

Letter Health Consultation

Indoor Air Exposure Evaluation for a Residential Plastic Manufacturing Unit in Dauphin County, Pennsylvania.

April 2022



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Letter Health Consultation: A Note of Explanation

A Letter Health Consultation/Health Consultation is a verbal or written response from the Agency for Toxic Substances Disease (ATSDR) or ATSDR's Cooperative Agreement Partners to a specific request for information about health risks related to a specific site, a chemical release, or the presence of hazardous material. To prevent or mitigate exposures, a consultation may lead to specific actions, such as restricting the use of or replacing water supplies, intensifying environmental sampling, restricting site access, or removing the contaminated material.

In addition, consultations may recommend additional public health actions, such as conducting health surveillance activities to evaluate exposure or trends in adverse health outcomes, conducting biological indicators of exposure studies to assess exposure, and providing health education for health care providers and community members. This concludes the health consultation process for this site unless additional information is obtained by ATSDR or ATSDR's Cooperative Agreement Partner, which, in the Agency's opinion, indicates a need to revise or append the conclusions previously issued.

The Pennsylvania Department of Health (PA DOH) prepared this Letter Health Consultation for residents of a Residential Plastic Manufacturing Unit in Dauphin County, Pennsylvania. This publication was made possible by grant number CDC-RFA-TS17-170103CONT19 from ATSDR. The PA DOH evaluated data sampled/monitored/estimated using approved methods, policies, and procedures existing at the date of publication.

PA DOH evaluated the available data of known quality for this Letter Health Consultation using approved methods, policies, and ATSDR procedures existing at the date of publication. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of ATSDR or the U.S. Department of Health and Human Services.

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To:

The Concerned Resident
Dauphin County, Pennsylvania.

Dear Resident:

This Letter Health Consultation (LHC) is written in response to your health concerns expressed to the Agency for Toxic Substances and Disease Registry (ATSDR) and the Pennsylvania Department of Health (PADOH). Per your concern, your ex-spouse has been manufacturing large amounts of plastics in the basement of the residence (“the site”), and your family, particularly children, have been experiencing a variety of health issues, such as skin rashes, gastro-intestinal (GI) issues, sleep issues, vomiting blood, breathing issues, neurological issues, and other related health symptoms. You were also concerned about genetic effects (DNA alteration) and sought information about a test for the DNA alterations due to exposures to contaminants at the residence.

Per the information shared, four residents (one adult male, one adult female, and two children) resided continuously at the site for 5 years (2012-2017). You (the female adult) stopped residing in 2017 but in 2018, your two children started living at the site intermittently for 3 days in every other weekend. On October 15, 2020, the Menz Industrial Hygiene Services (MIHS) collected the indoor air samples from the residence. Their report (the “MIHS Report”) concluded that quantifiable concentrations of environmental contaminants, including acetone vapor, styrene vapor, and airborne fibers, were detected in the samples. This letter provides a health effects and risks evaluation of the exposure to the detected contaminants of the MIHS Report and provides recommendations for the four residents.

PADOH concludes that the adult male is at risk of neurological and neuro-behavior health effects of acute (less than 15 days) and intermediate (15 -365 days) exposures of acetone (28.51 mg/m³) inhalation, but there are insufficient data to determine the health effects of maximum acute or intermediate exposures for styrene or airborne fibers inhalations in the past. For chronic (long-term, more than 365 days) exposures, all four residents at the site could be at higher risk for neurological health effects due to the detected level of styrene inhalation (3.92 mg/m³). Chronic exposure to acetone (28.51 mg/m³) is also expected to have neurological and neurobehavior health risks to all four residents. In the absence of sufficient data, PADOH is unable to determine the toxicity from exposures to the airborne fibers. PADOH could not determine the cancer risk and the potential for DNA damage (genotoxicity) from these estimated acute and chronic inhalation exposures. PADOH is unable to suggest a test that would be specific enough to detect levels of these specific contaminants in the body or that could indicate genotoxic effects in the four residents from the inhalation exposures that have occurred at the site.

PADOH recommends that the plastic manufacturing be moved out or halted at the residence to prevent human exposure to the harmful contaminants. Children and adults should not be living in or visiting the building where the plastic manufacturing unit is located. As the four residents have been exposed to the indoor air-contaminants in the past while residing at the site, PADOH recommends they have regular medical visits for any neurological and neurobehavior health issues.

The remainder of this LHC contains detailed information explaining PADOH’s exposure analysis, its conclusions, and recommendations.

THE SITE BACKGROUND INFORMATION

A Pennsylvania resident (an adult female) contacted the Agency for Toxic Substances and Disease Registry (ATSDR) and called the Pennsylvania Department of Health (PADOH) on October 2nd, 2020 with health concerns about her children. The background information described here is based on notes from the conversations. The resident lived at the residence (“the site”) in Dauphin County, Pennsylvania with her husband from March 2012 until June 2017, and their two children were born during that period. Her ex-husband has been manufacturing large amounts of plastics (for car parts) in the basement of the residence at least since 2012. The citizen’s family, particularly her children, have been experiencing a variety of health issues including skin rashes, gastrointestinal issues, sleep issues, vomiting blood, breathing issues, neurological issues, and other symptoms. After June 2017 the female resident moved out with her children and is no longer living at the site. After moving out, she didn't let her children visit the site for a year, and during that period she and her children didn't experience these health issues.

In October 2018, the children began staying at the site intermittently every other weekend (3 out of every 14 days). After a month, the children began having similar health issues again with symptoms such as cough, itchy skin, rashes, nosebleeds, and anxiety; consequently, they needed to visit doctors regularly. The female resident spoke to a medical attorney who directed her to contact PADOH. She informed PADOH that she had been court-ordered to get medically tested, and a doctor in Williamsport, Pennsylvania diagnosed her son with a mood dysregulation disorder due to a frontal lobe inhibition. The doctor stated that exposure to organic solvents can cause frontal lobe inhibition, and the exposures at the site could be a potential cause for her son’s diagnosis. The resident also stated that sanded fiberglass particles were everywhere in the residence. She expressed concerns that styrene and acetone are known to cross the placenta and can transmit through breast milk, that spontaneous abortion is a side effect of styrene exposure, and her daughter (younger child) was born prematurely. The resident sought information on DNA tests for detecting any genetic alterations due to exposure to chemicals from her ex-husband’s plastic manufacturing operations.

On October 15, 2020, Menz Industrial Hygiene Services (MIHS) collected acetone vapor, styrene vapor, and airborne fiber samples from the residence’s manufacturing shop in the basement, and from the kitchen area above the manufacturing shop (in the residential living space). In response to the resident’s concerns, the PADOH prepared and shared a technical assistance document in March 2021 recommending that the resident’s ex-husband either move the plastic manufacturing outside the residence or meet their children at an alternate location. In July 2021, PADOH was informed that the resident’s ex-husband agreed to move the plastic manufacturing out of the residence. However, at the time of drafting this Letter Health Consultation, PADOH has no confirmation that the plastic manufacturing had been moved out; as such, PADOH assumed that exposures were ongoing at the site.

PADOH evaluated the exposures by reviewing the MIHS sampling data, evaluating exposure pathways, and calculating exposure concentrations for the detected indoor air contaminants at the site, as described in the following sections.

CONTAMINANTS – DATA OF INDOOR AIR SAMPLES

On October 15, 2020, MIHS visited the site and collected indoor air samples. The samples were collected from the manufacturing shop in the basement and from the kitchen area above the manufacturing shop. The samples were analyzed by an accredited laboratory, EMSL Analytical Inc., Cinnaminson, New Jersey, for styrene, acetone, airborne fibers, and common particle identification of bulk material as per standard protocols [MIHS Report 2020]; the details of the sample collections are provided in Appendix B. Table 1 displays the detected indoor air concentrations from the acetone vapors, styrene vapors, and airborne fibers samples.

Table 1. Detected Concentrations of Indoor Air Contaminants in the Samples from the MIHS Report

| Location | Acetone* mg/m ³ (ppm) | Styrene* mg/m ³ (ppm) | Airborne fibers f/cc |
|--|-------------------------------------|-------------------------------------|-------------------------|
| In manufacturing shop, near worktable | 28.51 (12.0) | 3.92 (0.92) | <0.0278 f/cc |
| In kitchen, near rear door and love seat | 4.75 (2.0) | 0.81 (0.19) | 0.0221 f/cc |
| In kitchen, near rear door and love seat (D) | 5.71 (2.4) | -- | -- |
| QA Blanks | ND | ND | <5.5 fibers/100 fields |

** for conversion from ppm unit to mg/m³ refer Appendix A; ppm – parts per million; mg/m³ – milligram per cubic meter; f/cc – fibers per cubic centimeter; D – duplicate sample; ND – Not detected*

As described in the next section, PADOH evaluated exposure pathways to determine how the detected contaminants could come into contact with human subjects.

EXPOSURE PATHWAY EVALUATION FOR INDOOR AIR CONTAMINANTS

The evaluation of the exposure pathway determines if a contaminant is, has been, or will come into contact with a population. A typical exposure pathway analysis evaluates an exposure within the context of five exposure elements – the source, the environmental medium, exposure point, exposure route, and the exposed population [ATSDR 2005]. These five elements determine to what extent exposure may have occurred, may be occurring, or may occur in the future at and around a site. An exposure pathway is categorized as completed, potential, or eliminated. A completed exposure pathway is the one in which all the five elements are present. Additional details on exposure pathways are provided in Appendix C.

Inhalation Exposure Pathway: Contaminants were detected in the indoor air samples. Therefore, to determine whether the four residents (a male adult, a female adult, and two children) at the site had been, are currently, or would likely be exposed in the future by inhalation, PADOH evaluated the exposure pathway's five elements. The evaluation is summarized in Table 2.

From the evaluation, PADOH identified that all five elements of the exposure pathway were present in the past, present, and could be present in the future (if the plastic manufacturing is not moved out). PADOH concluded that a completed inhalation exposure pathway existed for the indoor air contaminants - acetone, styrene, and airborne fibers - from the residents' breathing in the contaminated indoor air; hence, the past exposure pathway is completed for all four residents, who lived at the site from March 2012 until June 2017. So, PADOH deemed the past exposure pathways completed, and the present and future exposure pathways as "potential" if the manufacturing is not moved out, which would result in continued exposures for the adult male and two children (Table 2).

Table 2: Inhalation Exposure Pathway Evaluation for the Site

| Elements of Exposure Pathway | | | | | Exposure Pathway Types | Conclusion for Exposure Pathway |
|---|------------------------------|-------------------------|-------------------|-----------------------------------|--|---------------------------------|
| 1. Contaminant Source | 2. Fate and Transport Medium | 3. Exposure Point | 4. Exposure Route | 5. Potentially Exposed Population | | |
| Manufacturing of plastics in the basement at the site | Air | Contaminated indoor air | Inhalation | Residents | Past (March 2012 – June 2017; & Oct 2018 – Dec 2021) | Completed |
| | | | | | Present (2022) | Potential |
| | | | | | Future (after 2022) | Potential |

Dermal Exposure Pathway: The sampled indoor air contaminants may have the potential to be absorbed through skin. However, sufficient evidence such as absorption factors for the contaminants is not available. Therefore, PADOH is unable to evaluate the dermal exposure pathway for the site contaminants.

Another potential exposure pathway at the site is through contaminated clothing worn by the adult male (ex-husband of the resident and father of the two children) during the plastic manufacturing and brought into the kitchen, living and bedroom areas of the residence. The contaminated clothes could off-gas the contaminants and expose the residents. But at this point, we are unable to evaluate this pathway as we do not know the exact concentration that could off-gas from the clothes.

As described in the next section, PADOH further evaluated the indoor air contaminants to determine whether the site-specific exposures could result in adverse health effects for the adults and the children at the site. The evaluation includes determination of Contaminants of Concern (COCs) through data screening, identification of an exposure unit, and calculations of exposure point concentrations (EPC).

SCREENING AND EVALUATION OF THE CONTAMINANTS OF CONCERN AT THE SITE

PADOH screened the MIHS report’s indoor air sampling data per ATSDR’s Public Health Guidance Manual [2005] against the recommended ATSDR’s health-based comparison values (CVs) to identify the contaminants that required further evaluation. CVs include environmental media evaluation guides (EMEGs), reference dose media evaluation guides (RMEGs), and cancer risk evaluation guides (CREGs). EMEGs are estimated contaminant concentrations in specific media (air, water, soil) that are not expected to result in adverse non-cancerous health effects after exposure for a given period, such as an acute (14 days or less), intermediate (15 to 365 days), or chronic (365 days or more) period. The EMEGs are based on ATSDR minimal risk levels (MRLs) for a given period (acute, intermediate, and chronic). An MRL is an ATSDR estimate of daily human exposure to a hazardous substance at or below which the substance is unlikely to pose a measurable risk of non-cancerous health effects. The RMEGs are based on EPA’s reference dose (RfD) and are estimated contaminant concentrations at which a chronic human exposure is not likely to result in adverse noncarcinogenic effects. The RfD is an EPA estimate of the

daily dose of a substance over a lifetime of exposure that is unlikely to cause harm to humans. The CREGs are estimated contaminant concentrations expected to cause no more than one excess cancer case in a million people (1 in 1,000,000) exposed during a lifetime of 78 years [ATSDR 2005].

These guides (RMEGs, EMEGs, CREGs) are derived from data drawn from published epidemiologic and toxicologic literature with many uncertainties or safety factors applied to ensure that they are amply protective of human health. If the detected maximum concentration of a contaminant exceeds the health-based screening value, it is selected as a COC and further evaluated. When an ATSDR CV is not available, screening values are acquired from federal or state environmental agencies' medium-specific concentration or cleanup standards (e.g., EPA, PADEP, Texas Commission on Environmental Quality (TCEQ)). However, the bases for values obtained from the environmental agencies were not reviewed/approved by ATSDR. If the contaminant does not have a CV or if the contaminant is of citizen concern, it is also selected as a COC [ATSDR 2005].

In the MIHS report, the indoor air samples (2-3 for each contaminant) were collected from two locations at the site: the plastic manufacturing shop in the basement and the kitchen area above the manufacturing shop. The detected concentrations were highest in the manufacturing shop, and there was no information on access restrictions to the shop. Therefore, as per ATSDR's recommendations on reasonable maximum exposure (RME), PADOH considered the maximum concentrations detected at the site for its COC screening process [ATSDR 2020].

Contaminants of Concern (COCs): Per ATSDR guidance [ATSDR 2005], any contaminant whose maximum concentration at the site exceeds the CV, is of citizen concern, or does not have a CV is selected as a COC. The determination of a COC does not necessarily indicate adverse health effects will occur but that the COC requires further evaluation [ATSDR 2005]. For COCs, PADOH derives an EPC to account for site-specific exposure.

Table 3 displays the maximum indoor air concentration of contaminants detected at the site and their respective ATSDR-recommended CVs or other agency screening level to determine if the sample(s) meet the criteria for being selected as a COC for further evaluation. If no ATSDR recommended CV was available, we used other agencies health-based effect screening level (ESL) values (e.g., TCEQ 2015).

Table 3: Comparing the Site's Maximum Indoor Air Contaminants with Comparison Values (CVs)

| Contaminant (Exposure Type) | Maximum Concentration (in mg/m ³) | Recommended CV (in mg/m ³) | CV Type | Selected for Further Evaluation |
|-----------------------------|---|--|--------------------------|---------------------------------|
| Acetone (Chronic)* | 28.51 | 4.80 | TCEQ Chronic ESL* | Yes |
| Acetone (Acute) | 28.51 | 19.00 | ATSDR Acute EMEG | Yes |
| Styrene (Chronic) | 3.92 | 0.85 | ATSDR Chronic EMEG / MRL | Yes |
| Styrene (Acute) | 3.92 | 21.00 | ATSDR Acute EMEG | No |
| Airborne Fibers | 0.0221 (fiber/cc) | Not available | Not applicable | Yes |

Notes: * acetone was selected, though no chronic ATSDR EMEG/MRL is available but there is a chronic Effect Screening Level (ESL) from for Texas Commission on Environmental Quality (TCEQ 2015) for Acetone; CV – Comparison Value; mg/m³ – milligram per cubic meter; fiber/cc – fiber per cubic centimeter; EMEG - environmental media evaluation guide; RMEG - reference dose media evaluation guide; MRL - minimal risk levels; samples were collected for 30 min for Acetone, and 60 min for Styrene; also refer to the Appendix D for screening in the ATSDR PHAST, Ver 2.0.1.0.

Per Table 3, there is no chronic ATSDR CV for acetone, but the acetone's maximum detected concentration exceeds the chronic value of the Texas Commission on Environmental Quality (TCEQ)'s chronic health effect screening level [TCEQ 2015] and exceeds the ATSDR's acute CV; hence, PADOH considered acetone as a COC. For styrene, the detected maximum concentration exceeded ATSDR's CV, thus it is a COC. There is no ATSDR CV for airborne fibers; hence, PADOH retained airborne fibers as a COC. These identified COCs were further evaluated.

Exposure Unit(s) at the site: As per ATSDR guidance [ATSDR 2005], the exposure unit needs to be defined first to derive the site-specific EPC. A typical exposure unit is an area where a person has contact with an environmental medium, such as soil, surface water or inhaled air containing the COC. A site could have more than one exposure unit depending on the nature of the exposure(s) and access restrictions at the site. At this site, the plastic manufacturing shop is in the basement. The two adults and two children had lived at the site, and now one adult male and two children continue to live intermittently at the site. But without any access restrictions for adults or children to the plastic manufacturing shop at the site, the entire site (residence) is considered as one single exposure unit [ATSDR 2020] for the past, present, and future inhalation exposures (if manufacturing is not moved out).

Exposure Point Concentrations for the COCs at the Site: PADOH calculated exposure point concentrations (EPCs) for the detected COCs to determine whether site-specific exposures were high enough, frequent enough, and lasted for a long enough period to result in adverse health effects [ATSDR 2005]. PADOH calculated the inhalation air EPCs in accordance with ATSDR EPC guidance [ATSDR 2019] and followed the ATSDR's recommended assumptions (provided in Appendix F) for residential inhalation [ATSDR 2020] of indoor air contaminants.

To determine EPCs, PADOH followed ATSDR's inhalation guidance [ATSDR 2020] for evaluating inhalation exposures for each of the four residents. Per the guidance, PADOH calculated adjusted EPC for chronic inhalation. Hereafter in this document, PADOH refers to EPCs as adjusted EPCs to account for the duration, frequency, and time of exposure at the site. The maximum detected concentrations were used for assessing acute or short-term exposures. PADOH considered appropriate exposure factors specific to each of the four residents for chronic, intermediate, or acute exposures (Appendix G). The details of the assumptions, exposure factors, and adjusted EPC calculations are provided in Appendices F-H.

In this health assessment, based on the COCs (Table 3), PADOH considered acute (less than 15 days) and chronic (long-term, more than a year) exposures for acetone, and only chronic exposures for styrene for all four residents. The residents had continuously lived at the site for many years, the adult male continues to live at the site full time and the children may continue to visit the site intermittently for the foreseeable future. The maximum detected acetone concentration exceeded its respective health-based acute and chronic exposure CV and styrene concentration only exceeded the chronic CV (Table 3). It is possible that higher peaks of styrene exposures could have occurred in the past; however, no data are available to assess the styrene acute exposures. It is also likely that the residents reported health symptoms may be associated with both acute and chronic exposures to styrene, acetone, or both.

Calculations of Adjusted EPCs for COCs exposures: To estimate site-specific inhalation exposures, PADOH calculated adjusted EPCs for acetone and styrene exposures for the four residents. Airborne fibers do not have a CV or MRL; therefore, PADOH did not calculate adjusted EPCs for airborne fibers.

After adjusting for total period of exposures (Appendices F & G), PADOH calculated adjusted EPCs for each of the four residents based on the maximum detected acetone (28.51 mg/m³) and styrene (3.92 mg/m³) concentrations at the site and presented in Table 4.

Table 4. Adjusted EPCs for Inhalation Exposures of COCs for Each Resident at the Site

| Residents | Site Specific Exposure Factors | Acetone adjusted EPC* (mg/m ³) | Styrene adjusted EPC** (mg/m ³) |
|---------------|--------------------------------|--|---|
| Male-adult | 1.00 | 28.51 | 3.92 |
| Female-adult | 0.50 | 14.26 | 1.96 |
| Older-child | 0.57 | 16.29 | 2.24 |
| Younger-child | 0.52 | 14.76 | 2.03 |

*based on maximum detected acetone concentration at site - 28.51 mg/m³; and **maximum detected styrene concentration - 3.92 mg/m³

As described in the next section, PADOH evaluated the potential health effects (non-cancer and cancer) from inhalation exposures to these COCs by assessing their exposure levels (adjusted EPCs) for each resident and by reviewing known toxicological information of the COCs from published research.

ACETONE INHALATION EXPOSURE - TOXICOLOGICAL EVALUATIONS

The maximum detected acetone concentration (28.5 mg/m³) was above the ATSDR’s recommended acute inhalation CV (19.0 mg/m³). ATSDR does not have chronic CV or MRL for acetone inhalation, so PADOH used screening values from other states or from the EPA. The Texas Commission on Environmental Quality (TCEQ) has long-term (chronic) health effect screening level (ESL) of 4.8 mg/m³ for acetone inhalation. Using the available screening levels, PADOH conducted a toxicological evaluation and calculated site-specific acetone inhalation adjusted EPCs and HQs for chronic and acute exposures for each resident. PADOH further evaluated the known acetone toxicological information from published studies to estimate the chronic exposure risks and non-cancer and cancer health effects.

Acetone: Acetone is a colorless, highly volatile, water-soluble liquid with a distinct smell and taste. People begin to smell acetone in the air at 100 to 140 ppm (237.55 – 332.56 mg/m³), but some people can smell it at much lower levels. Acetone is found naturally in the environment and produced by industries. Low levels of acetone are normally present in the body from the breakdown of fat. In industrial settings, acetone is used to make plastics, fibers, and drugs. Acetone is also used as a solvent to dissolve other substances [ATSDR 2021].

Acetone occurs naturally in plants, trees, volcanic gases, and forest fires. People and animals exhale acetone produced from the natural breakdown of fat. Acetone is released during its manufacturing and use, and from automobile exhaust, tobacco smoke, landfills, and the burning of waste materials. Acetone is lost in the air when it reacts with sunlight and other chemicals. Rain and snow remove small amounts of acetone from the atmosphere and deposit it on land and in water. Ambient acetone level in cities is generally higher than in rural areas. The typical outdoor air acetone level is about 7 ppb (0.017 mg/m³) and slightly higher in indoor air (8 ppb or 0.019 mg/m³) in cities in the United States, probably due to the indoor use of household chemicals [ATSDR 2021].

Acetone is readily absorbed by the lungs and gastrointestinal tract and can be absorbed dermally. Acetone is metabolized to glucose in the liver and subsequently excreted as carbon dioxide. In the human body, acetone has very little tendency to accumulate and is generally eliminated within 1-3 days.

Acetone and acetone-derived carbon dioxide are excreted mostly in the expired breath. Small amounts are also excreted in urine. Babies and individuals with certain health conditions, such as pregnancy, diabetes, have higher acetone levels in their body. The higher acetone levels don't usually cause any health problems. The most prominent effects of acetone inhalation are eye and respiratory tract irritation, and neurobehavioral health effects [ATSDR 2021]. Per Occupational Safety and Health Administration (OSHA) regulations for the United States, workers should not be exposed to levels higher than 750 ppm (1,781.6 mg/m³). As most people can smell acetone in the air at 100 to 140 ppm (237.55 – 332.56 mg/m³), means people will probably smell acetone before they feel any effects, like headache and confusion [ATSDR 2021].

Acetone Inhalation Exposure – estimation of non-cancer risks: ATSDR does not have a chronic inhalation MRL for acetone, but the acetone's maximum detected concentration (28.51 mg/m³) exceeds the chronic value of the TCEQ's chronic health effect screening level of 4.8 mg/m³ [TCEQ 2015; Appendix J] and exceeds ATSDR's recently added acute CV of 19.0 mg/m³ [ATSDR 2021; Appendix J]. These chronic and acute CVs will be used to assess health risks. At the site, adjusted EPCs for acetone exposure were 28.51 mg/m³ for the male adult, 14.26 mg/m³ for the female adult, 16.29 mg/m³ for the older child, and 14.76 mg/m³ for the younger child (Table 4). These calculated adjusted EPCs were used to derive each resident's chronic and acute exposures hazard quotients (HQs) to assess the potential for health risks. The HQ is the ratio of the estimated exposure concentration to the MRL (Table 5). The higher the concentration (above the MRL), the greater the chance for noncancerous health effects. If the HQ is less than 1.0, noncancerous health effects are unlikely to occur. If an HQ exceeds 1.0, the exposure dose concentrations are compared to levels in scientific literature that have caused adverse health effects in human epidemiological studies.

Table 5. Calculations of Hazard Quotients for Acetone Exposures

| Resident | Acetone Adjusted EPC (mg/m ³) | Chronic HQ (Adjusted EPC/MRL ^a) | Acute HQ (Adjusted EPC/MRL ^b) |
|---------------|---|---|---|
| Male-adult | 28.51 | 6.0 | 1.5 |
| Female-adult | 14.26 | 3.0 | 0.8 |
| Older-child | 16.29 | 3.4 | 0.9 |
| Younger-child | 14.76 | 3.1 | 0.8 |

^a - TCEQ chronic MRL of 4.8 mg/m³; ^b - ATSDR acute MRL of 19.0 mg/m³ for acetone.

PADOH calculated chronic and acute HQs for each resident by dividing the site-specific adjusted EPCs by the TCEQ chronic inhalation MRL for acetone of 4.8 mg/m³ and ATSDR acute inhalation MRL for acetone of 19.0 mg/m³ (Table 5). The chronic HQs for the male adult (6.0), female adult (3.0), older child (3.4) and younger child (3.1) were all above 1.0. For acute exposure, only the male adult (1.5) had HQ > 1.0. The HQ > 1.0 indicates that exposure could have adverse health effects; thus, PADOH compared these exposures to available studies in the scientific literature.

PADOH evaluated the chronic health effects by reviewing a study by Satoh et al. (1996) on health effects of chronic acetone exposure [Satoh et al 1996; TCEQ 2015]. This study examined the neurotoxic effects of acetone in 110 male workers at three acetate fiber plants and in 67 nonexposed male plant workers as controls. The mean exposure duration was 14.9 years for the acetone-exposed workers. Symptoms of eye irritation, tearing, and nausea were reported by 13.7-45.1% of the exposed workers during or after work vs. 3.9-23.5% of the unexposed workers (controls). Over six months of prior acetone exposure,

23.6-25.8% of exposed workers reported neurological symptoms such as heavy feelings in the head, faint feelings, and nausea than 2.9-9.8% of controls. The difference between exposed and controls were statistically significant. No significant differences in hematological parameters, neutrophil phagocytic activity, or serum biomarkers of liver function, were observed between groups [Satoh et al 1996; TCEQ 2015].

PADOH evaluated the acute health effects by reviewing the acute health effect study by Dick et al (1989) [Dick et al 1989; ATSDR 2021]. The study exposed 11 male and 11 female volunteers to acetone (237 ppm; or 570 mg/m³) for 4 hours. The acute-duration inhalation MRL of 19.0 mg/m³ (8 ppm) is based on a minimal LOAEL of 570 mg/m³ for neurobehavioral effects after application of an uncertainty factor of 30 - 3 for use of a minimal LOAEL and 10 for human variability [ATSDR 2021; Appendix J]. Acetone-exposed participants showed significant increases in response time (p <0.05) and significantly greater false alarm percentages (p <0.005) on the auditory tone discrimination task compared to controls. In addition, significant increases in measures of anger and hostility were observed in males, but not females, exposed to acetone (p <0.001), however, this may be due to the small sample size and absence of any other significant changes in mood tests [ATSDR 2021; Dick et al 1989]. Similar effects (lack of energy, general weakness, delayed visual reaction time, and headache) have also been observed in humans exposed to 250 ppm (593.9 mg/m³) acetone for 6 hours or repeatedly for 6 hours/day for 6 days [Matsushita et al. 1969a, 1969b]. Another study by Muttray et al. (2005) reported the neurological effects among acetone-exposed male volunteers at 247 ppm (587.7 mg/m³) for 4.5 hours.

Other studies suggest that workers and people exposed to acetone reported nose, throat, lung, and eye irritation. Some people feel this irritation at 100 ppm (237.55 mg/m³) acetone level in the air [ATSDR 2021]. Women workers exposed to acetone at workplace reported having a shortened menstrual cycle [Stewart et al. 1975; Lin et al 2013]. In another study [Nizyaeva 1982], pregnant women workers exposed to indoor air acetone from 14 to 126 ppm (33.26 -299.31 mg/m³) were reported to have increased incidences of pregnancy complications, including miscarriage, toxicosis, decreased hemoglobin levels, hypotension, and “weakness of labor activity,” compared to the unexposed workers. Increased incidences of developmental effects, such as intrauterine asphyxia of fetuses and decreased weight and length of neonates, were also reported in pregnant exposed women workers. However, the number of women assessed, description of the exposed and unexposed workers (such as age, smoking history, use of alcohol), description of workroom monitoring, and statistical methods were not reported in the study; hence, the conclusions were uncertain [ATSDR 2021].

As reviewed above, the neurological effects of acetone inhalation exposure range from dizziness and headaches to dulling of reflexes, anger, and hostility. At the site, the chronic acetone exposures with HQs > 1.0 suggest that all four residents are at risk of chronic neurological health effects. The adult male is also at risk of increased neurological and neuro-behavioral health effects from acute short-term acetone exposures.

Acetone Inhalation Exposure - estimation of cancer risks: There are very limited epidemiological studies between acetone exposures and cancer in humans. Retrospective mortality studies found no excess risk of death from cancer in exposed workers [Ott et al. 1983a, 1983b]. Another case-control study [Kerr et al. 2000] found an association between pediatric neuroblastoma risk and maternal exposure to acetone but the study may have recall bias impacting the results [ATSDR 2021]. No animal studies have been associated with any increases in neoplastic lesions or cancer. Due to the lack of data

concerning carcinogenicity in humans and animals, the EPA has classified acetone in Group D, which is not classifiable as to human carcinogenicity [EPA 2003]. The IARC and the NTP have not classified acetone as a carcinogen [ATSDR 2021]. The cancer risks are calculated using the adjusted EPC and inhalation unit risk (IUR) for a chemical; however, no IUR is currently available for acetone. Hence, the cancer risk from acetone exposure could not be estimated for the four residents at the site (Appendix Table I-2).

Acetone Inhalation Exposure - sensitive population at the site: At the site, two pregnancies occurred, and two neonates/children and one female of reproductive age resided. Neonates and pregnant women are considered sensitive populations. Multiple factors, such as genetic makeup, developmental stage, age, health, and nutritional status (including inconsistent diets or nutritional deficiencies), make certain populations more sensitive to exposure to environmental contaminants. These factors may result in decreased function of the detoxification and excretory processes (mainly hepatic, renal, and respiratory). For example, the youngest of the population with immature and developing organs will generally be more vulnerable to toxic substances than healthy adults. A sensitive population will exhibit a different or enhanced response to acetone than most persons exposed to the same level of acetone in the environment. No human acetone exposure study on sensitive populations is available, but some animal studies are reviewed below.

In a lethality study among newborns, 14-day-old, and adult rats, susceptibility to the lethal effects of acetone generally decreased with increasing maturity [Kimura et al. 1971]. In another study, pregnant rats exposed to acetone inhalation during gestation had reduced body weights; however, nonpregnant rats exposed to a higher concentration for a longer duration did not have the effect on body weights [Goldberg et al. 1964]. Pregnant rats also had lower levels of acetone metabolism in plasma and liver than virgin rats [Peinado et al. 1986], suggesting differences in the acetone metabolism in pregnant rats.

Animal studies indicate sex differences in the susceptibility to acetone exposure. For example, male rats were more susceptible than female rats to acetone's hematological, hepatic, renal effects, and effects on reproductive organs [ATSDR 2021; NTP 1991]. Humans may have a similar susceptibility, and acetone exposure may exacerbate preexisting hematological, liver, kidney, or reproductive disorders, though animal studies cannot always be extrapolated to humans. Therefore, in the absence of any conclusive human study, PADOH is unable to determine whether the adult female would have been more susceptible during her pregnancies or whether her two children are more susceptible to acetone chronic inhalation exposures to the maximum detected acetone concentration of 28.51 mg/m³ at the site.

Acetone Inhalation Exposure – genotoxicity: Currently, no conclusive human or animal study is available on the genotoxic effects of acetone inhalation exposure; however, two studies associated genotoxicity with occupational acetone exposures. A study by Heuser et al. (2005) showed the mean cytogenetic damage index was significantly greater for workers using solvent-based adhesives than for water-based adhesives and control groups [Heuser et al 2005]; however, the solvent-based adhesives consisted primarily of toluene rather than acetone. Another study by Pitarque et al. (1999) did not show excess DNA damage in workers exposed to a mixture of solvents including acetone relative to controls [Pitarque et al. 1999]. In vitro studies of bacteria and cultured animal cells as well as human fibroblasts and skin epithelial cells, indicate that acetone is not likely to be genotoxic in humans [ATSDR 2021]. Therefore, the available evidence suggests that the acetone inhalation exposure at the site may not have significant genotoxic effects or DNA damage in the four residents.

STYRENE INHALATION EXPOSURE - TOXICOLOGICAL EVALUATIONS

PADOH evaluated site-specific inhalation exposures (adjusted EPCs) to styrene for each resident at the site and compared these exposures to published toxicological studies.

Styrene: Styrene is a colorless liquid that evaporates easily. Large amounts of styrene are produced in the United States, but small amounts are also produced naturally by plants, bacteria, and fungi. Styrene is present in cigarette smoke, photocopiers and printers' toners, and automobile exhaust. Indoor air levels of styrene in the USA have been reported in the range of 0.1– 50 $\mu\text{g}/\text{m}^3$ (0.0001 – 0.050 mg/m^3) and can be attributed mostly to emissions from building materials, consumer products, and tobacco smoke. The principal route of styrene exposure for the general population is by inhalation of contaminated indoor air. Usually, the workplace or home office has substantially higher levels of styrene in indoor air due to emissions from laser printers and photocopiers [ATSDR 2010]. Workers involved in styrene polymerization, rubber manufacturing, or working in styrene-polyester resin facilities or photocopy centers may be exposed to styrene. The most common health problems in styrene-exposed workers involve the nervous system, including changes in color vision, tiredness, feeling drunk, slowed reaction time, concentration problems, and balance problems. The styrene concentrations that cause these effects are more than 1,000 times higher than levels normally found in the environment [ATSDR 2010].

Styrene Inhalation Exposure – estimation of non-cancer risks: ATSDR has derived a chronic-duration MRL of 0.85 mg/m^3 for styrene inhalation [ATSDR 2010; Appendix J]. This MRL is based on a meta-analysis of occupational exposure studies demonstrating alterations in choice reaction time and color discrimination in styrene workers [Ska et al. 2003]. In the current investigation, the calculated site-specific styrene adjusted EPCs were 3.92 mg/m^3 for the male adult, 1.96 mg/m^3 for the female adult, 2.24 mg/m^3 for the older child, and 2.03 mg/m^3 for the younger child (Table 4). PADOH further evaluated the noncancerous health effects of inhaled styrene by calculating hazard quotients (HQs) for each of the four residents at the site. The HQ is the ratio of the estimated exposure concentration to the MRL. The higher the concentration (above the MRL), the greater the chance for noncancerous health effects. If an HQ exceeds 1.0, the exposure concentrations are compared to levels that have caused health effects in human epidemiological studies.

PADOH calculated HQs for each resident by dividing the site-specific adjusted EPCs by the ATSDR chronic inhalation MRL for styrene of 0.85 mg/m^3 (Table 6). The HQs for the male adult (4.61), female adult (2.31), older child (2.64), and younger child (2.39) were all above 1.0. The HQ > 1.0 indicates the exposure could have health effects; thus, PADOH compared these exposures to levels of significance exposures (LSE) studies in the scientific literature. Also, though the acute and intermediate levels of styrene were not measured but some of the health symptoms (neurological issues) described by the female resident for her children could be caused by acute exposure levels (> 5.0 ppm; 21.3 mg/m^3) of styrene at the site.

Table 6. Calculations of Hazard Quotients for Chronic Styrene Exposures

| Resident | Styrene Adjusted EPC (mg/m ³) | Chronic HQ (Adjusted EPC/MRL ^a) |
|---------------|---|---|
| Male-adult | 3.92 | 4.61 |
| Female-adult | 1.96 | 2.31 |
| Older-child | 2.24 | 2.64 |
| Younger-child | 2.03 | 2.39 |

^a - MRL= ATSDR chronic MRL of 0.85 mg/m³ for Styrene.

Styrene is an established neurotoxicant in occupational settings (ATSDR 2010). Most of the available information on the effects of styrene inhalation in humans is based on studies among exposed workers from the production or use of polyester resins dissolved in styrene. Several studies have characterized neuro-toxicity and health issues related to occupational exposure to airborne styrene in reinforced plastics manufacturing [Papaleo et al 2011; Strafella et al 2013; Triebig et al 1989]. In most of the studies [ATSDR 2010], the chronic styrene inhalation exposures ranged from 10 ppm (42.6 mg/m³) to 1000 ppm (4259.7 mg/m³). These concentrations are much higher than the highest detected concentration at the site (3.92 mg/m³). However, one study [Thiess and Fredheim 1978] found that workers exposed to <1 ppm (4.26 mg/m³) for 1-36 years had significantly lower percentages of hemoglobin and erythrocyte counts compared to the non-exposed (control) group, though the study had some uncertainties, such as concomitant exposures [ATSDR 2010]. The concentration of <1 ppm (4.26 mg/m³) with abnormal low hemoglobin and erythrocyte counts is comparable to the highest exposure (3.92 mg/m³) at the site. Per ATSDR (2010), the MRL study of 20 ppm (85.2 mg/m³) exposure [Benignus et al 2005] is selected as the point of departure for the chronic-duration styrene inhalation exposure to calculate the inhalation MRL (0.20 ppm; 0.85 mg/m³). The study [Benignus et al, 2005] suggests chronic (long-term, more than a year) styrene exposure may exert a variety of effects on the nervous system, including increased choice reaction time and color vision loss. Therefore, based on this evidence, the adult male, the adult female, the older child, and the younger child (with HQ > 1.0) at the site could be at higher risk for neurological health effects. Though the acute and intermediate levels of styrene were not measured, some of the health symptoms (neurological issues) being experienced by the resident’s children could be caused by the acute exposure level (> 5.0 ppm; 21.3 mg/m³) of styrene at the site.

Styrene Inhalation Exposure - estimation of cancer risks: The International Agency for Research on Cancer (IARC), and the National Toxicology Program (NTP) of the US Department of Health and Human Services have determined that styrene is probably/reasonably carcinogenic to humans [ATSDR 2010]. There are several epidemiologic studies which suggest there may be an association between styrene exposure and an increased risk of leukemia and lymphoma; however, the evidence is inconclusive due to multiple chemical exposures, inadequate documentation of the levels and durations of exposure to styrene, and small sample size of such studies. But the data are suggestive of some carcinogenic potential of styrene in humans [ATSDR 2010].

The U.S. EPA’s inhalation unit risk (IUR) is the incremental risk posed by a specific concentration unit in air (usually per 1 microgram per cubic meter (µg/m³) of the pollutant in the air). The calculation yields a relative increase in cancer risk (above the background rate) from exposure to individual pollutants [EPA 1992a]. Generally, cancer risk can be calculated by multiplying the adjusted EPCs by the IUR after adjusting the duration of exposure using the appropriate exposure factor calculation (Appendix G). At

this time, there is no EPA IUR for styrene; hence, the cancer risk from styrene exposure could not be estimated for the four residents at the site (Appendix Table I-1).

Styrene Inhalation Exposure - sensitive population at the site: Two pregnancies occurred, and two neonates/children and a reproductive-age female lived at the site. Neonates and pregnant women are considered sensitive populations. A sensitive population may exhibit a different or enhanced response to styrene than most persons exposed to the same level of styrene in the environment. However, occupational exposure studies have not found significant increases in the occurrence of stillbirth, infant death, malformations, or low birth weight [ATSDR 2010]. In male workers, sperm abnormalities have been reported, but not alterations in time-to-pregnancy or fertility rates [Kolstad et al. 2000]. In animal studies, an increase in fetal deaths was observed in hamsters exposed to very high concentrations (1,000 ppm or 4,259.71 mg/m³) on gestation days 6–18, and in rats exposed to 300 ppm (1,277.91 mg/m³) on gestation days 6–20 [Katakura et al. 2001]. In rats, no adverse reproductive effects were observed in inhalation and oral multigeneration studies [ATSDR 2010]. There are no health studies evaluating the effects of styrene exposure on children or any study on immature animals. Based on the evidence, PADOH cannot conclude whether the pregnant adult female (HQ of 2.14) and two children living at the residence (with HQs of 2.64 and 2.39) would be more sensitive than the male adult to health effects from chronic styrene inhalation exposure at the maximum concentration (3.92 mg/m³) at the site.

Styrene Inhalation Exposure – genotoxicity: In response to the citizen’s inquiry about the possibility of styrene-induced DNA damage in her children, PADOH evaluated available human studies. There is evidence for genotoxicity in styrene-exposed industrial workers based on detected markers of DNA damage such as chromosomal aberrations, sister chromatid exchanges, or micronuclei formation [ATSDR 2010]. But these genotoxic effects occurred at concentrations 20 to 100-fold (20 – 104 ppm or 85.19 – 443.01 mg/m³) higher than the maximum styrene concentration (3.92 mg/m³) detected at the site. There are no known studies on styrene exposure and DNA damage, and health effects in children. After reviewing the limited evidence, PADOH is unable to determine if long-term (more than 5 years’) chronic exposure to styrene (3.92 mg/m³) would cause significant DNA damage.

AIRBORNE FIBERS INHALATION EXPOSURE - TOXICOLOGICAL EVALUATIONS

The highest detected concentration of airborne fibers was 0.0221 fibers/cc (Table 3) at the site. There is no ATSDR’s recommended inhalation CV for airborne fibers; therefore, PADOH conducted the toxicological evaluation based on available studies on airborne fibers exposure.

A fiber is a long, slender particle. To be counted as a fiber, the particle must be at least 5 micrometers long (5 μm) and have an aspect ratio (ratio of a fiber’s length to its diameter) of at least 3 to 1 or sometimes 5 to 1. The diameter of a fiber is an important property because compared to thick fibers, very thin fibers are more easily suspended in air and can be breathed in and deposited deep in the lungs. Only very thin fibers with diameters less than 3 μm can be inhaled into the lower respiratory tract of the lungs. Thicker fibers are deposited on the mucous-lined surface of the upper respiratory tract, including the nose and mouth. Usually, glass wool, rock wool, slag wool, and refractory ceramic fibers have the smallest diameters, while continuous filament glass fibers have the largest diameters [ATSDR 2004].

Most of the available studies examined the health effects of exposure to synthetic vitreous fibers. These fibers are found in insulation glass wool or ceiling boards, rock (stone) wool, slag wool, and in continuous filament glass. Usually, workers who produce or use synthetic vitreous fiber-containing products, workers who install and come into contact with insulating material, or workers involved in building demolition, maintenance, and repair may be exposed to airborne fibers.

When inhaled, some of the airborne fibers will be deposited in the nasal and oral passages and on the surface lining of the lungs. Most fibers deposited in the nasal and upper lung airways are removed by being carried away in a layer of mucous to the throat, where they are swallowed into the stomach [ATSDR 2004]. Fibers deposited in the deepest parts of the lungs where gas exchange occurs are removed more slowly by macrophages. Macrophages can engulf the fibers and move them to the mucous layer and the larynx, where they can be swallowed. The swallowed fibers and macrophages are excreted in the feces.

Inhalation of fibers can cause chronic pleural diseases, pulmonary fibrosis, and lung cancers. Excess lung cancer and pulmonary fibrosis are caused by fibers that are longer than $\sim 20 \mu\text{m}$ [Lippmann 2015]. The U.S. EPA Integrated Risk Information System (IRIS) has not classified the potential carcinogenicity of glass wool, continuous filament glass, rock wool, or slag wool, but has deemed refractory ceramic fibers as a probable human carcinogen [EPA 1992b]. Though children breathe differently and have different lung structures than adults, it is unlikely that these differences will cause more fibers to remain in the lungs of children than adults. It is possible that exposure of young children to highly durable fibers could lead to pulmonary effects after very long latency periods but there is no evidence to support this possibility [ATSDR 2004].

At the site, airborne fibers were detected, and the maximum concentration was 0.0221 f/cc, but the fibers were of various types, including 12% unidentified particles, polyester fibers, and polyester fibers with an unidentified surface coating. There are no toxicity data for these types of airborne fibers. However, the mechanism could be similar for site airborne fibers as for synthetic vitreous fibers or the fibers described above, so interventions should be implemented at the site to eliminate or reduce human exposures to the airborne fibers. In the absence of specific and sufficient toxicity data, PADOH is unable to determine the toxicity of airborne fiber exposures among the four residents at the site.

COMPOSITE INHALATION EXPOSURES OF THE CONTAMINANTS - TOXICOLOGICAL EVALUATIONS

The four residents at the site are inhaling the air contaminated with acetone, styrene, and airborne fibers and are at risk of composite harmful effects of exposures to these contaminants. But information regarding interactions between acetone, styrene, and airborne fibers inhalation exposures are not known in humans. However, a few studies exploring co-exposures to acetone and styrene in humans have reported conflicting combined effects. A study of 19 male workers exposed to styrene and acetone in the air at work for 4-hour intervals reported an inverse correlation between the amount of acetone in the air and post-shift styrene metabolite levels in the urine of the exposed subjects, suggesting that acetone may slow metabolism of styrene [Marhuenda et al 1997]. However, in 23-34 years old men exposed for 2 hours to 293 mg/m^3 styrene alone or a mixture of 301 mg/m^3 styrene and $1,240 \text{ mg/m}^3$ (517 ppm) acetone, there was no indication that acetone alters the uptake, distribution, metabolism, or elimination of styrene [Wigaeus et al. 1984]. Based on this evidence, it is difficult to conclude if co-exposure to acetone (28.8 mg/m^3) and styrene (3.8 mg/m^3) at the site had additive or inverse health effects on the four residents.

TESTING INFORMATION FOR THE EXPOSURES

The citizen requested medical test information to determine whether she and her children had been exposed to the indoor contaminants. PADOH reviewed available information on testing and summarized it below:

Testing Information for Styrene Exposure: Styrene can be measured in blood, urine, and body tissues for a short time following exposure to moderate-to-high levels. The presence of styrene breakdown products (metabolites) in urine might indicate exposure to styrene. Measuring styrene metabolites in urine within 1 day of exposure allows medical personnel to estimate an actual exposure level. However, the metabolites can also form from exposures to other substances/chemicals. Therefore, detection of the metabolites in urine cannot be specifically attributed to the styrene exposure source.

Testing Information for Acetone Exposure: Acetone can be measured in exhaled air, blood, and urine. Methods for measuring acetone in breath, blood, and urine are available at most modern testing labs. Doctors' offices may not have the necessary equipment but can take blood and urine samples to send to a testing lab. However, normal acetone levels of acetone in breath, blood, and urine can vary widely depending on many factors, such as infancy, pregnancy, lactation, diabetes, physical exercise, dieting, physical trauma, and alcohol. Therefore, detection of higher levels of acetone through a test cannot be specifically attributed to the acetone exposure source.

Testing Information for Airborne Fibers Exposure: No tests are available that are specific enough to determine exposures to synthetic fibers. A chest x-ray is a common method to assess certain health conditions, such as pleural plaques, lung or pleural fibrosis, lung tumors, or mesotheliomas, but x-rays cannot show the presence of fibers in the lung.

LIMITATIONS AND UNCERTAINTIES

This letter health consultation's conclusions should be interpreted in the context of the following limitations, uncertainties, and assumptions. The collected samples may not represent of actual exposures; for example, when samples were collected, the manufacturing was suboptimal, and an air fan was used for ventilation, so the detected concentrations and exposures may be underestimated in this evaluation. Also, the samples were collected at one time, which might have missed possible short-term acute exposures and seasonal variations and fluctuations for a realistic estimation of the exposures. Though this one-time sampling did not account for the acute and intermediate levels of exposure, as higher peaks of styrene and acetone exposures could have occurred, but some of the health symptoms (neurological and neurobehavioral issues) described by the female resident could be caused by the acute exposure levels at the site. Additionally, in the absence of access restrictions information, this exposure evaluation assumes the maximum (reasonable maximum exposure, RME) detected concentration of the contaminants. But if access to the manufacturing shop was restricted for children and the adult female, then their exposure levels would be lower. Similarly, if manufacturing was limited to a certain number of hours per day, or a certain number of months per year, then the exposure factors would be less, and exposure risks would be lower. The residents reported health symptoms likely to be associated with both acute and chronic exposures to acetone and styrene alone and together. However, in the absence of conclusive evidence, the composite inhalation exposure risks of the contaminants could not be estimated. Additionally, sufficient information is not available on all the chemicals used, and their stored quantities at the site. So, if there are additional chemicals and if

chemicals are not stored and secured (Appendix E) in a recommended manner at the site, then additional chemical exposures and additional exposures through dermal and/or ingestion pathways could have occurred but could not be evaluated in this health assessment.

CONCLUSIONS

Based on the exposure calculations and toxicological evaluations but with limited samples, PADOH concludes that the adult male at the site is at risk of neurological health effects. But the three residents (the adult female and two children) are unlikely to be at health risk from the acute acetone inhalation exposures. There are insufficient styrene data to determine the maximum acute exposures and their durations in the past; hence, PADOH is unable to evaluate acute or intermediate styrene exposures and their health effects. Assuming detected levels of acetone and styrene are chronic and long-term, all four residents at the site are at risk for neurological health effects caused by chronic acetone and chronic styrene inhalation exposures. In the absence of sufficient toxicity data for airborne fibers, PADOH is unable to determine the toxicity from this exposure. Also, PADOH could not determine cancer risk and DNA damage or genotoxicity among the four residents for the chronic inhalation exposures. Additionally, no information is available on a medical test that could conclusively detect the level of contaminants in the body attributable to the site or any test that could conclusively indicate genotoxicity in the four residents from the exposures to the contaminants (acetone, styrene, airborne fibers) at the site.

RECOMMENDATIONS

1. As per the information in July 2021, PADOH recommends that the plastic manufacturing be moved out or halted at the residential site, and all chemicals and activities related to plastic manufacturing be moved out to a location where proper ventilation is available to protect from harmful human exposures to the contaminants.
2. If the plastic manufacturing cannot be stopped or moved out of the residential site, then PADOH recommends that:
 - i. Children not to visit or reside at the site.
 - ii. The site to have restricted access for children altogether and adults who lack personal protective equipment (PPE) when accessing the plastic manufacturing area.
 - iii. Per existing OSHA guidance (<https://www.osha.gov/plastic-industry/hazards-solutions>), the access to the site be restricted, proper ventilation be ensured, and the adult male resident to use PPE during the plastic manufacturing to limit and reduce the exposures.
 - iv. All chemicals (Appendix E) used for manufacturing at the site be properly stored and secured to avoid any spillover and additional exposures.
 - v. For any future exposure evaluation, if needed, environmental monitoring should be conducted under various conditions to obtain a refined assessment of exposure conditions and exposure pathways to all possible contaminants. Such conditions include: 1) sampling during a typical manufacturing process during which time-weighted concentrations will be evaluated for the hours of operation; and 2) sampling at different seasons or multiple times in a year. In addition, information should be provided for typical operation hours and manufacturing months during a year, and a complete list of all stored/used chemicals for the plastic manufacturing.
3. All four residents are recommended to have regular medical visits for any neurological and neurobehavior health issues that may be result from past styrene and acetone exposures at the site.

Sincerely,

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REFERENCES AND CITED SOURCES

- ATSDR (2004). Agency for Toxic Substances and Disease Registry – Toxicological profile for Synthetic Vitreous Fibers. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <https://www.atsdr.cdc.gov/ToxProfiles/tp161.pdf>
- ATSDR (2005). Agency for Toxic Substances and Disease Registry - Public Health Assessment Guidance Manual. https://www.atsdr.cdc.gov/hac/phamanual/pdfs/phagm_final1-27-05.pdf
- ATSDR (2010). Agency for Toxic Substances and Disease Registry – Toxicological profile for Styrene. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <https://www.atsdr.cdc.gov/ToxProfiles/tp53.pdf>
- ATSDR (2019). Agency for Toxic Substances and Disease Registry - Exposure Point Concentration Guidance for Discrete Sampling, V2. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, July 12, 2019.
- ATSDR (2020). Agency for Toxic Substances and Disease Registry - Guidance for Inhalation Exposures, V3. Atlanta, Ga: U.S. Department of Health and Human Services, Public Health Service, December 1, 2020.
- ATSDR (2021). Agency for Toxic Substances and Disease Registry - Toxicological profile for Acetone. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <https://www.atsdr.cdc.gov/ToxProfiles/tp21.pdf>
- Dick RB, Setzer JV, Taylor BJ, et al. (1989). Neurobehavioural effects of short duration exposures to acetone and methyl ethyl ketone. *Occup Environ Med* 46(2):111-121.
- EPA (1992a). Integrated Risk Information System (IRIS): Chemical Assessment for Styrene; CASRN 100-42-5; https://iris.epa.gov/static/pdfs/0104_summary.pdf
- EPA (2003). Integrated Risk Information System (IRIS); Toxicological Review for Acetone; CASRN 67-64-1; <https://iris.epa.gov/static/pdfs/0128tr.pdf>
- EPA (1992b). Integrated Risk Information System (IRIS); Toxicological Review for Refractory ceramic fibers; CASRN – none found; https://iris.epa.gov/static/pdfs/0647_summary.pdf
- Goldberg E, Johnson E, Pozzani C, et al. (1964). Effect of repeated inhalation vapors of industrial solvents on animal behavior. *Am Ind Hyg Assoc J* 25:369-375.
- Heuser VD, de Andrade VM, Silva J, et al. (2005). Comparison of genetic damage in brazilian footwear-workers exposed to solvent-based or water-based adhesive. *Mutat Res* 583(1):85-94.
- Katakura Y, Kishi R, Ikeda T, et al. (2001). Effects of prenatal styrene exposure on postnatal development and brain serotonin and catecholamine levels in rats. *Environ Res* 85(1):41-47.
- Kerr MA, Nasca PC, Mundt KA, et al. 2000. Parental occupational exposures and risk of neuroblastoma: a case-control study (United States). *Cancer Causes Control* 11(7):635-643.
- Kimura T, Ebert M, Dodge W. (1971). Acute toxicity and limits of solvent residue for sixteen organic solvents. *Toxicol Appl Pharmacol* 19:699-704.

- Kolstad A, Bisanti L, Roeleveld N, et al. (2000). Time to pregnancy among male workers of the reinforced plastics industry in Denmark, Italy and the Netherlands. *Scand J Work Environ Health* 26(4):353-358.
- Lin CC, Huang CN, Hwang YH, et al. (2013). Shortened menstrual cycles in LCD manufacturing workers. *Occup Med (Lond)* 63(1):45-52.
- Lippmann, M. (2015). Toxicological and epidemiological studies on effects of airborne fibers: coherence and public health implications. *Crit Rev Toxicol.* 2015; 45(1):92.
- Matsushita T, Goshima E, Miyagaki H, et al. (1969a). Experimental studies for determining the mac value of acetone: 1. biological reactions in the "one-day exposure" to acetone. *Sangyo Igaku* 11(10):477-484.
- Marhuenda D, Prieto MJ, Periago JF, et al. (1997). Biological monitoring of styrene exposure and possible interference of acetone co-exposure. *Int Arch Occup Environ Health* 69(6):455-460.
- Matsushita T, Goshima E, Miyagaki H, et al. (1969b). Experimental studies for determining the mac value of acetone: 2. biological reactions in the "six-day exposure" to acetone. *Sangyo Igaku* 11(10):507-515.
- MIHS Report (2020). MENZ Industrial Hygiene Services (File # 2020.116): Final Report - October 15, 2020 Evaluation and Exposure Sampling at Sunbeam Drive, Dauphin County, Pennsylvania.
- Muttray A, Martus P, Schachtrup S, et al. (2005). Acute effects of an organic solvent mixture on the human central nervous system. *Eur J Pharm Med Res* 10(9):381-388.
- Nizyaeva IV. (1982). The hygienic evaluation of acetone. *Gig Tr Prof Zabol (Russian)* 6:24-28.
- NTP (1991). National Toxicology Program - technical report no. 3. Toxicity studies of acetone in F344/N rats and B6C3F, mice (drinking water studies). Research Triangle Park, NC: U.S. National Institute of Health. NIH publication no. 91-3122.
- OSHA - Occupational Safety and Health Administration - Safety and Health Topics - Plastics Industry <https://www.osha.gov/plastic-industry/hazards-solutions>
- Ott MG, Skory LK, Holder B, et al. 1983a. Health evaluation of employees occupationally exposed to methylene chloride: General Study design and environmental considerations. *Scand J Work Environ Health* 9(Suppl 1):1-38.
- Ott MG, Skory LK, Holder B, et al. 1983b. Health evaluation of employees occupationally exposed to methylene chloride: Mortality. *Scand J Work Environ Health* 9(Suppl 1):1-38.
- Papaleo B, Caporossi L, Bernardini F, Cristadoro L, Bastianini L, De Rosa M, et al. Exposure to styrene in fiberglass-reinforced plastic manufacture: still a problem. *J Occup Environ Med.* 2011;53(11):1273-8. [PubMed: 21926918]
- Peinado J, Lopez-Soriano J, Argiles M. (1986). The metabolism of acetone in the pregnant rat. *Biosci Rep* 6:983-989.
- PHAST (2022). Public Health Assessment Site Tool (PHAST, Ver 2.0.1.0.) Comparison Values Screen for Acetone and Styrene in Air.

- Pitarque M, Vaglenov A, Nosko M, et al. (1999). Evaluation of DNA damage by the Comet assay in shoe workers exposed to toluene and other organic solvents. *Mutat Res* 441(1):115-127.
- Satoh T, Omae K, Nakashima H, Takebayashi T, Matsumura H, Kawai T, et al. (1996). Relationship between acetone exposure concentration and health effects in acetate fiber plant workers. [Comparative Study Research Support, Non-U.S. Gov't]. *Int Arch Occup Environ Health*, 68(3), 147-153
- Ska B, Vyskocil A, Tardif R, et al. (2003). Effects of peak concentrations on the neurotoxicity of styrene in volunteers. *Hum Exp Toxicol* 22:407-415.
- Strafella E, Bracci M, Staffolani S, Manzella N, Giantomasi D, Valentino M, et al. Occupational styrene exposure induces stress-responsive genes involved in cytoprotective and cytotoxic activities. *PLoS One*. 2013;8(9):e75401.
- Stewart D, Hake L, Wu A, et al. (1975). Acetone: Development of a biologic standard for the industrial worker by breath analysis. Cincinnati, OH: National Institute for Occupational Safety and Health. NTIS PB82-172917.
- TCEQ (2015). Texas Commission on Environmental Quality (TCEQ) – Acetone; Development Support Document. revised September 2015.
- Thiess M, Friedheim M. (1978). Morbidity among persons employed in styrene production, polymerization and processing plants. *Scand J Work Environ Health* 4 (Suppl 2):203-214.
- Triebig G, Lehl S, Weltle D, Schaller KH, Valentin H. (1989). Clinical and neurobehavioural study of the acute and chronic neurotoxicity of styrene. *Occup Environ Med* 46(11):799–804
- Wigaeus E, Löf A, Nordqvist MB. (1984). Uptake, distribution, metabolism, and elimination of styrene in man. A comparison between single exposure and co-exposure with acetone. *Occup Environ Med* 41(4):539-546.

Appendix A

Conversion Equations used for the concentrations of acetone and styrene from parts per million (ppm) into milligram per cubic meter (mg/m³) or vice-versa¹:

PPM to mg/m³ = Y mg/m³ = (X ppm) x (molecular weight)/24.45; Fill in either the "ppm" value (X) or the "mg/m³" value (Y) AND the molecular weight of the compound.

The conversion equation is based on 25 °C and 1 atmosphere

Molecular weight of styrene = 104.15 g/mol

Molecular weight of acetone = 58.08 g/mol

Conversion of PPM (0.92) to mg/m³ for Styrene: (0.92 X 104.15/24.45) = 3.92 mg/m³

Conversion of PPM (12) to mg/m³ for Acetone: (12 X 58.08/24.45) = 28.51 mg/m³

1 Parts Per Million (PPM) = 1000 Part Per Billion (PPB)

¹<https://cfpub.epa.gov/ncer/abstracts/index.cfm/fuseaction/display.files/fileid/14285>

Appendix B

Acetone Vapors Samples Collection: Three acetone vapor samples were collected in accordance with *NIOSH Method 1300* with a flow rate of 0.1 – 0.2 liters per minute (lpm) for a maximum volume of 3 liters in a sorbent media. These samples were collected at 0.1 lpm for 30 minutes. One sample was collected from the plastic manufacturing shop in the basement and two samples were collected from the kitchen area (above the manufacturing area) for the analysis.

Styrene Vapors Samples Collection: Two styrene vapor samples were collected in accordance with *NIOSH Method 1501* with a flow rate of less than 1.0 lpm for a maximum volume of 14 liters in a sorbent media. The samples were collected at 0.2 lpm for 60 minutes. One sample was collected from the manufacturing shop in the basement and one sample was collected from the kitchen area (above the manufacturing area).

Airborne fibers Samples Collection: Two airborne fibers were collected in accordance with *NIOSH Method 7400* using mixed cellulose ester filter cassettes with 0.8-micron pores. One sample was collected from the manufacturing shop in the basement and one sample was collected from the kitchen area (above the manufacturing area) for the analysis.

Appendix C

Exposure Pathway Description: An exposure pathway is a description of the route/path of environmental contaminants that are released from the source, how and where they move, and then how people can come into contact with and/or become exposed them. The exposure pathway evaluation determines if the contaminants are, have been, or will be in contact with local populations. A typical exposure pathway evaluates the contaminant exposures in the context of the following five elements [ATSDR 2005]:

Element 1: The contaminant source or release - the sources may include industrial facilities, landfills, and many others which may release contaminants into various media.

Element 2: Environmental fate and transport - once released to the environment, contaminants move through and across different media (water, soil, or air) and some may degrade altogether.

Element 3: Exposure point - this is the specific location(s) where people might have the contact with a contaminated medium (ambient air, private residential well water, indoor air).



Element 4: Exposure route - the route is how people physically contact environmental contamination at the exposure point (by inhalation, ingestion, or through dermal contact).

Element 5: Potentially exposed populations – to identify and characterize populations (residents, children, workers) that may come or may have encountered contaminants.


Exposure pathways are categorized as completed, potential, or eliminated. A completed exposure pathway is the one in which all five elements are present. In a potential exposure pathway, at least one of the elements is uncertain, indicating that exposure to a contaminant could have occurred in the past, is occurring, or could occur in the future. A pathway is eliminated when one or more elements are missing or prevented and are unlikely to be present.


Appendix D


Screening the Comparison Values for Acetone and Styrene in Air from Public Health Assessment Site Tool (PHAST, Ver 2.0.1.0.)

| ATSDR Screening Values | | | | | | | | | |
|--|--------|-----------|---------------------------------|-----------------------------|------|--------------|----------|-----------|------------|
| Contaminant Name / CASRN | Conc | Unit | Above or Equal to Rec ATSDR CV? | Above or Equal to Other CV? | CREG | Chronic EMEG | Int EMEG | RMEG | Acute EMEG |
| Acetone 67-64-1 | 28,510 | µg/m³ | NA | NA | NA | NA | NA | NA | 19,000 [3] |
| Styrene  100-42-5 | 3,920 | µg/m³ | Yes [1] | Yes [2] | NA | 850 [1] | NA | 1,000 [2] | 21,000 |
| Fibrous glass and mineral wool  NULL-CAS-002 | 0.0221 | fibers/cc | NA | NA | NA | NA | NA | NA | NA |

Note: Inhalation EMEGs and the RMEG are equivalent to duration-specific inhalation MRLs and RFC, respectively.

 (1) Recommended ATSDR CV met or exceeded.

 (2) Additional ATSDR CV met or exceeded.

 (3) Acute ATSDR CV met or exceeded.

| Select Contaminant(s) for Further Evaluation | | | | | | | | |
|--|-----------------|-------------------|-----------|----------------------|------------------|---------------------------------|-------------------------------------|-------|
| Contaminant Name | Exposure Medium | Maximum Site Conc | Unit | ATSDR Recommended CV | ATSDR CV Type | Selected for Further Evaluation | Select for Exposure Calculator | Notes |
| Acetone | Air | 28,510 | µg/m³ | 19,000 | Acute EMEG/MRL | Yes | <input checked="" type="checkbox"/> | |
| Styrene | Air | 3,920 | µg/m³ | 850 | Chronic EMEG/MRL | Yes | <input checked="" type="checkbox"/> | |
| Fibrous glass and mineral wool | Air | 0.0221 | fibers/cc | NA | NA | Yes | <input type="checkbox"/> | |

Appendix E

Site specific photographs from MENZ Industrial Hygiene Services of chemical storage in the residence (File # 2020.116): Final Report - October 15, 2020 Evaluation and Exposure Sampling, Dauphin County, Pennsylvania.



Pic 1: Credits: MENZ Industrial Hygiene Services



Pic 2: Credit: MENZ Industrial Hygiene Services

Appendix F

Assumptions and Methodology Used to Calculate Exposure Factors for all Four Residents of the Site:

At the site, all four residents, including two adults (a male and a female) and two children inhaled the indoor air contaminated with the detected contaminants of concern (COCs) - acetone, styrene, and airborne fibers. At least one adult and two children could continue to inhale the COCs in indoor air at the site if the plastic manufacturing is not moved out. The two newborns and now children had lived and continue to live intermittently (over every other weekend; 3 out of 14 days) since 2018 till 2021 at the site. PADOH used following guidelines and assumptions to evaluate the potential adverse health effects of the exposures for the two children and for the two adults:

- ATSDR recommends the use of an average life expectancy value of 78 years for adults (both males and females), but for assessments where exposures are gender-specific, life expectancy values of 75 years for men and of 80 years for women are recommended.
- The exposure factor (EF) for residential scenarios is generally assumed to be daily (24 hours a day, 365 days a year), resulting in an EF = 1 for non-cancer residential health outcomes and an appropriately adjusted EF for cancer residential health outcomes (the site-specific exposure duration over a lifetime, in years).
- The adult male lived and continue to live at the site (no adjustment in exposure factor of 1).
- The adult female lived at the site for five years (2012 – 2017).
- The older child lived at the site for four years until 2017, and then after one year of not living in or visiting the home, the older child lived in the home 3 out of every 14 days (every other weekend) from 2018 until present (2021).
- The younger child lived at the site for three years until 2017, and then after one year of not living in or visiting the home, the younger child lived in the home 3 out of every 14 days (every other weekend) from 2018 until present (2021).

Equation to Calculate Exposure Factors: An exposure factor (EF) expresses how often (frequency) and how long (duration) a person might contact a contaminant in the environment by using following equation:

$$EF = (F \times ED) / AT$$

Where, "F" is exposure frequency, "ED" is exposure duration, and "AT" is averaging time. The default EF value is usually 1, which indicates exposure occurs daily for acute, intermediate, and chronic durations.

Residential Inhalation Assumptions: According to the ATSDR guidance [ATSDR 2020], PADOH assumes children and adults are exposed 24 hours a day, 7 days a week, 52.14 weeks a year. PADOH assumes the detected highest concentrations at the site, and as this is a continuous residential exposure scenario and the plastic manufacturing in the residence has been occurring since 2012, PADOH assumes the exposures are long-term and the stayed at the same level.

The daily air intake rates (m³/day) for children and adults account for variation in breathing/ventilation rates (m³/min or m³/hour) during typical activities during the day, but these ventilation rates are not generally used to evaluate exposure unless inhalation exposure occurs during a specific activity, such as intense physical exertion [ATSDR 2020]. Therefore, PADOH did not use different ventilation rates for children and adults in exposure factor calculations in this residential site.

Appendix G

1) Non-cancer Exposure Factors Calculations for the Site: Considering the reasonable maximum exposure (RME) conditions for past 10 years (2012 – 2021), a typical EF for non-cancer chronic residential exposure is:

$$EF_{\text{non-cancer chronic}} = [(24 \text{ hr/day}) \times (7 \text{ day/week}) \times (52.14 \text{ week/year}) \times 10 \text{ years}] / [(24 \text{ hr/day}) \times (7 \text{ day/week}) \times (52.14 \text{ week/year}) \times 10 \text{ years}] = 1$$

But considering each resident's occupancy history in the residence, PADOH calculated the EFs for chronic past and present exposures for the site-specific conditions for each of the four residents as following:

- Male Adult: Past Exposure factor (2012 – 2021): $(24 \text{ hr}/7 \text{ days}/365 \text{ days}) - 10 \text{ years} = 1$
- Male Adult: Present Exposure Factor for Male Adult at the residence: $(24 \text{ hr}/7 \text{ days}/365 \text{ days}) = 1$

- Female Adult: Past Exposure factor (2012 – 2017): $(24 \text{ hr}/7 \text{ days}/365 \text{ days}) - 5 \text{ years} = 1$
- Female Adult: No Present Exposure Pathway (2021); eliminated.

- Older Child: Past Exposure factor (2013-2017), $24 \text{ hr}/7 \text{ days}/365 \text{ days}$, at least for 4 Years = 1
- Older Child: Past Exposure factor (2018-2021): 3 days in every other weekend at the residence: $3/14 = 0.214$ (for at least 4 Years)

- Younger Child: Past Exposure factor (2014-2017), $24 \text{ hr}/7 \text{ days}/365 \text{ days}$, at least for 3 Years = 1
- Past Exposure factor Younger Child (2018-2021): 3 days in every other weekend at the residence: $3/14 = 0.214$ (at least 4 Years)

- Both Children: Present Exposure Factor for 3 days in every other weekend at the residence: $3/14 = 0.214$

2) Calculations of Non-cancer Assessment Exposure Factors for the Four Residents:

$$EF_{\text{adult-male, chronic-noncancer}} = [(24/24) \times (7/7) \times (52.14/52.14) \times (10)] / [(24/24) \times (7/7) \times (52.14/52.14) \times (10)] = 1$$

$$EF_{\text{adult-female, chronic-noncancer}} = [(24/24) \times (7/7) \times (52.14/52.14) \times (5)] / [(24/24) \times (7/7) \times (52.14/52.14) \times (10)] = 0.50$$

$$EF_{\text{child-older, chronic-noncancer}} = [((24/24) \times (7/7) \times (52.14/52.14) \times (4)) + ((24/24) \times (3/14) \times (52.14/52.14) \times (4))] / [(24/24) \times (7/7) \times (52.14/52.14) \times (9)] = 0.5714$$

$$EF_{\text{child-younger, chronic-noncancer}} = [((24/24) \times (7/7) \times (52.14/52.14) \times (3)) + ((24/24) \times (3/14) \times (52.14/52.14) \times (4))] / [(24/24) \times (7/7) \times (52.14/52.14) \times (8)] = 0.5179$$

By considering above, the non-cancer assessment exposure factors for chronic residential exposure at the site since 2012 four residents were calculated (Appendix D3) and are as following:

$$\text{Sum of } EF_{\text{adult-male}}: [1 \text{ (for both past \& present exposures)}] = 1$$

$$\text{Sum of } EF_{\text{adult-female}}: [1 \text{ (only for past 5 years)}] = 0.5$$

$$\text{Sum of } EF_{\text{child-older\#1}}: [1 \text{ (for past 4 years)} + 0.214 \text{ (past 4 Years)}] = 0.57$$

$$\text{Sum of } EF_{\text{child-younger\#2}}: [1 \text{ (for past 3 years)} + 0.214 \text{ (past 4 Years)}] = 0.52$$

Appendix H

EPCs and HQs Equations used for the Site:

1) Equation used for Calculation of Adjusted Exposure Point Concentrations: To determine EPCs, PADOH followed ATSDR's guidance [ATSDR 2020] for evaluating inhalation exposures for all four residents (one male adult, one female adult, one older child, one younger child) by calculating the adjusted exposure point concentration (adjusted EPC) by an appropriate exposure factor for all four residents for chronic, intermediate, or acute exposure. PADOH adjusted EPC to account for the duration, frequency, and time of exposure in the residence by following adjusted EPC formula:

Adjusted EPC = (C x EF); where Adjusted EPC = Adjusted Exposure Point Concentration ($\mu\text{g}/\text{m}^3$), C = Contaminant's Concentration ($\mu\text{g}/\text{m}^3$), EF = Exposure Factor (unitless)

2) Equation used for Calculation of Hazard Quotients (HQs) for the Four Residents of the Site: Using the site-specific EFs for the residents of the site, PADOH compared the adjusted EPCs to the ATSDR chronic inhalation MRL to calculate hazard quotients for long term chronic exposures for the four residents using the following equation:

$$\text{HQ} = \text{Adjusted EPC (mg/m}^3\text{)}/\text{Inhalation MRL (mg/m}^3\text{)}$$

The HQ for a contaminant of concern is the ratio of the estimated exposure dose to the MRL. If the HQ is less than 1.0, noncancerous harmful effects are unlikely to occur [ATSDR 2005]. If a HQ exceeds 1.0 the exposure dose concentrations are then compared to levels in the scientific literature that cause health effects in laboratory animals and human epidemiological studies.

Appendix I

1) Equation used for Exposure Factors for Cancer Assessment: In similar conditions and considering the RME conditions of residential occupancy of 33 years for an average life expectancy of 78 years, the EF for cancer assessment is:

$$EF_{\text{cancer, chronic}} = [(24 \text{ hr/day}) \times (7 \text{ day/week}) \times (52.14 \text{ week/year}) \times 33 \text{ years}] / [(24 \text{ hr/day}) \times (7 \text{ day/week}) \times (52.14 \text{ week/year}) \times 78 \text{ years}] = 0.42$$

2) Calculations of Exposure Factors for Cancer Assessment: ATSDR recommends the use of an average life expectancy value of 78 years for adults (both males and females), but for assessments where exposures are gender-specific, life expectancy values of 75 years for men and of 80 years for women are recommended. Using above formula and life expectancy values of 75 years for the male and of 80 years for the female, the cancer assessment exposure factors were calculated for each of four residents for chronic residential inhalation exposure since 2012 and are as below:

$$\text{Sum of } EF_{\text{adult-male-cancer}} = [(24/24) \times (7/7) \times (52.14/52.14) \times (10)] / [(24/24) \times (7/7) \times (52.14/52.14) \times (78)] = 0.13$$

$$\text{Sum of } EF_{\text{adult-female-cancer}} = [(24/24) \times (7/7) \times (52.14/52.14) \times (5)] / [(24/24) \times (7/7) \times (52.14/52.14) \times (80)] = 0.063$$

$$\text{Sum of } EF_{\text{child-older-cancer}} = [((24/24) \times (7/7) \times (52.14/52.14) \times (4)) + ((24/24) \times (3/14) \times (52.14/52.14) \times (4))] / [(24/24) \times (7/7) \times (52.14/52.14) \times (78)] = 0.062$$

$$\text{Sum of } EF_{\text{child-younger-cancer}} = [((24/24) \times (7/7) \times (52.14/52.14) \times (3)) + ((24/24) \times (3/14) \times (52.14/52.14) \times (4))] / [(24/24) \times (7/7) \times (52.14/52.14) \times (78)] = 0.0495$$

3) Calculations for Cancer Risks for Inhalation Exposure: Using the cancer exposure factors as calculated above and the adjusted EPCs, the excess risks were estimated by following equation:

$$\text{Cancer risk} = \text{IUR} \times \text{EPC} (\mu\text{g}/\text{m}^3) \times \text{EF}$$

Table I-1. Calculations of Excess Cancer Risk for Styrene Exposures

| Resident | Styrene Adjusted EPC (mg/m ³) | Site Specific Cancer Exposure Factor (EF) | Excess Cancer Risk (IUR) ^a |
|---------------|---|---|---------------------------------------|
| Male-adult | 3.92 | 0.13 | Not Available |
| Female-adult | 1.96 | 0.063 | |
| Older-child | 2.24 | 0.062 | |
| Younger-child | 2.03 | 0.05 | |

^a=cancer risk estimates based on inhalation unit risk (IUR) for cancer, but none is available for styrene

Table I-2. Calculations of Excess Cancer Risk for Acetone Exposures

| Resident | Acetone Adjusted EPC (mg/m ³) | Site Specific Cancer Exposure Factor (EF) | Excess Cancer Risk (IUR) ^a |
|---------------|---|---|---------------------------------------|
| Male-adult | 28.51 | 0.13 | Not Available |
| Female-adult | 14.26 | 0.063 | |
| Older-child | 16.29 | 0.062 | |
| Younger-child | 14.76 | 0.05 | |

^a=cancer risk estimates based on inhalation unit risk (IUR) for cancer, but none is available for acetone.

Appendix J

Levels of Significant Exposure (LSE) tables and Calculations of MRLs for Inhalation Exposure: ATSDR have developed the levels of significant exposure (LSE) tables and figures for toxicological evaluations of the contaminants of concerns [ATSDR 2010]. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. The LSE tables and figures also contain an estimate of levels posing minimal risk to humans known as Minimal Risk Levels or (MRLs) from which the Hazard Quotients (HQs) are calculated.

Styrene MRL: From the styrene LSE table, the LOAEL was classified as a minimal LOAEL based on Triebig et al., (2001) in which the exposure to the styrene led to the alterations in color vision but the alteration was reversible [ATSDR 2010]. In a meta-analysis [Benignus et al. 2005], the LOAEL of 20 ppm from Triebig et al. (2001) was selected as the point of departure for the chronic-duration styrene inhalation MRL of 0.20 ppm. The LOAEL was adjusted for intermittent exposure (8 hours/day, 5 days/week) and divided by an uncertainty factor of 30 (3 for use of a minimal LOAEL and 10 for human variability), resulting in a chronic-duration inhalation MRL of 0.2 ppm.

Acetone Chronic MRL: ATSDR does not have a chronic inhalation MRL for acetone. In the absence of ATSDR's chronic MRL, we used the Texas Commission on Environmental Quality (TCEQ)'s chronic health effect screening level (4.8 mg/m³). TCEQ used a chronic health effect study [Sato et al 1996] that examined the neurotoxic effects of acetone in 110 male workers at three acetate fiber plants and in 67 nonexposed male plant workers as controls. Mean exposure duration was 14.9 years for the acetone exposed workers. The range of these daily breathing zone exposures was wide (5 - 1,212 ppm), with an overall mean of 361.4 ppm. Based on these findings, the TCEQ tentatively identifies the midpoint of the moderately-exposed group (375 ppm) as the LOAEL for neurological effects (e.g., heavy feelings in the head, faint feelings, nausea) from this study for purposes of deriving the chronic reference value (ReV). The LOAEL of 375 ppm happens to be not appreciably different from the overall mean (361.4 ppm) associated with neurological and irritation effects in this study. As this was an occupational study, the occupational exposure level must be adjusted to an environmental exposure level applicable to the public. Thus, the LOAEL value of 375 ppm was used to calculate a point of departure (POD) adjusted for the human equivalent concentration (POD_{HEC}).

$$\text{POD}_{\text{HEC}} = \text{PODOC} \times (\text{VE}_{\text{ho}}/\text{VE}_{\text{h}}) \times (\text{days per week}_{\text{oc}}/\text{days per week}_{\text{res}})$$

where: VE_{ho} = occupational ventilation rate for an 8-h day (10 m³/day); VE_{h} = nonoccupational ventilation rate for a 24-h day (20 m³/day); $\text{days per week}_{\text{oc}}$ = occupational weekly exposure frequency (study specific); $\text{days per week}_{\text{res}}$ = residential weekly exposure frequency (7 days per week), therefore, $\text{POD}_{\text{HEC}} = 375 \text{ ppm} \times 10 \text{ m}^3/20 \text{ m}^3 \text{ day} \times 5\text{d}/7\text{d}$; or

$$\text{POD}_{\text{HEC}} = 375 \text{ ppm} \times (10/20) \times (5/7) = 133.9 \text{ ppm}$$

The default for noncarcinogenic effects is to determine a POD_{HEC} and apply uncertainty factors (UFs) to derive a ReV. The UFs were applied to the POD_{HEC} of 133.9 ppm (duration-adjusted LOAEL) for neurotoxic effects in humans to calculate the chronic ReV. A total UF of 20 was applied to the POD_{HEC} , including 10 for intraspecies human uncertainty factor (UF_H), 2 for LOAEL to NOAEL uncertainty factor (UF_L), and 1 for incomplete database uncertainty factor (UF_D) to determine the chronic ReV.

$$\text{Chronic ReV} = 133.9 \text{ ppm} / 20 = 6.69 \text{ ppm (6,690 ppb, or } 16,000 \mu\text{g/m}^3\text{)}$$

This chronic ReV is expected to be protective of not only the potential chronic neurotoxic effects of acetone, but also potential effects associated with shorter-term exposure. The chronic ReV is then used to calculate the $\text{chronicESL}_{\text{threshold (non-cancer)}}$. At the target hazard quotient of 0.3, the Chronic REeV was multiplied by 0.3 to account for cumulative and aggregate risk during the air permit review.

$$\text{chronicESL}_{\text{threshold (non-cancer)}} = 2,000 \text{ ppb or } 4,800 \mu\text{g/m}^3 \text{ (or } 4.8 \text{ mg/m}^3\text{)}$$

Acetone Acute MRL: The ATSDR acute MRL was derived from the minimal LOAEL of 237 ppm for neurological effects (auditory tone discrimination task and neurobehavioral effects) in humans exposed to acetone for 4 hours (Dick et al. 1989). The study exposed 11 male and 11 female volunteers to acetone (237 ppm) for 4 hours. Exposed participants showed significant differences on two neurobehavioral tasks as compared to controls. Acetone-exposed participants showed significant increases in response time ($p < 0.05$) and significantly greater false alarm percentages ($p < 0.005$) on the auditory tone discrimination task compared to controls. The changes in performance on this task were persistent and mirrored the measured blood concentrations of acetone, indicating that tolerance to acetone did not occur [Dick et al 1989].

The LOAEL of 237 was divided by a total uncertainty factor of 30 (3 for use of a minimal LOAEL and 10 for human variability) was applied.

$$\text{Acute MRL} = \text{LOAEL} \div \text{UF} = 237 \text{ ppm} \div 30 = 8 \text{ ppm (or } 19.0 \text{ mg/m}^3\text{)}$$

Benignus VA, Geller AM, Boyes WK, et al. (2005). Human neurobehavioral effects of long-term exposure to styrene: A meta-analysis. *Environ Health Perspect* 113:532-538.

Dick RB, Setzer JV, Taylor BJ, et al. (1989). Neurobehavioural effects of short duration exposures to acetone and methyl ethyl ketone. *Occup Environ Med* 46(2):111-121.

Satoh T, Omae K, Nakashima H, Takebayashi T, Matsumura H, Kawai T, et al. (1996). Relationship between acetone exposure concentration and health effects in acetate fiber plant workers. [Comparative Study Research Support, Non-U.S. Gov't]. *Int Arch Occup Environ Health*, 68(3), 147-153

Triebig G, Stark T, Ihrig A, et al. (2001). Intervention study on acquired color vision deficiencies in styrene-exposed workers. *J Occup Environ Med* 43(5):494-500.