Community Cancer Incidence Data Review

B. Braun Medical Sterilization Facility

Allentown, Lehigh County, Pennsylvania

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Summary and Statement of Issues

INTRODUCTION	Through a cooperative agreement with the Agency for Toxic Substances and Disease Registry (ATSDR), the Pennsylvania Department of Health's (PA DOH) priority is to ensure that the community around the B. Braun facility has the best information possible to protect its health. In July 2019, ATSDR received a petition letter from U.S. Representative Susan Wild requesting a health consultation evaluating the potential health impacts from exposure to ethylene oxide (EtO) emissions for communities located near the B. Braun facility in Lehigh and Northampton Counties. However, currently there are no real-time EtO air monitoring data available for the facility to evaluate the potential health impacts. In August 2019, ATSDR acknowledged the petition and stated that it would collaborate with PA DOH and prepare a review report **on the incidence of cancer near the B. Braun facility**. The PA DOH analyzed historical cancer incidence data (1985 to 2017) from the Pennsylvania Cancer Registry for the population living within a 2-mile radius from the facility. All cancer cases within this area were geocoded. At the time of this cancer data review, geocoded cancer data was available through calendar year 2017. Age-adjusted standardized incidence ratios (SIRs) for three time-periods (1985-1994, 1995-2004, and 2005-2017) were used to examine the incidence of cancer types often associated with EtO exposure among this population relative to a reference population that lived outside of the 2-mile radius around the B. Braun facility within Lehigh and Northampton Counties. These cancer types included adult lymphohematopoietic cancers (Non-Hodgkin's lymphoma, Hodgkin's lymphoma, myeloma, and lymphocytic leukemia), adult female breast cancer, and all childhood/pediatric cancers (anyone diagnosed before 20 years of age with leukemia, brain tumors, lymphomas, Wilms tumor, bone and soft tissue cancer, and other pediatric cancers).
CONCLUSIONS	PA DOH reached the following two conclusions:
Conclusion 1	Age-adjusted cancer incidence rates, when analyzed by time-period and gender, did not present a consistent pattern. Unstable cancer rates were found and are most likely due to the small sample size (cancer rates based on the population within a 2-mile radius). The cancer rates observed in our analysis are not consistent with cancer patterns often associated with environmental exposure.

Basis for Conclusion	Our cancer analysis within a 2-mile radius of the site revealed no consistent pattern for adult lymphohematopoietic and female breast cancer rates between 1985-2017: • Male lymphohematopoietic cancer rates were higher (7% and 11% respectively) between 1985-1994 and 1995-2004 compared to the reference area but none were statistically higher. For the time-period 2005-2017, male lymphohematopoietic cancers were statistically lower (17%). • Female lymphohematopoietic cancers were higher (9%, 11%, and 2% respectively) for all three time-periods, but none were statistically higher. • Female breast cancer rates were lower (6%) between 1985-1994, higher (6%) between 1995-2004, and lower (5%) between 2005-2017 but none of these rates were statistically higher or lower. We observed similarly inconsistent patterns in childhood cancer rates: • Male childhood cancers within 2 miles of the facility were lower (17%) than the reference area between 1985-1994 and higher (9% and 11% respectively) between 1995-2004 and 2005-2017, but none of these rates were statistically lower or higher. • Female childhood cancers were statistically higher (88% and 84% respectively) than the reference area from 1985-1994 and 2005-2017. However, from 1995-2004, female childhood cancers were slightly lower (2%) than the reference area and were not statistically lower. There is no consistent pattern of cancer incidence rates among adults or children living within a 2-mile radius of the B. Braun facility relative to adults and children living outside the 2-mile radius. Difference in cancer rates indicate that the finding is more likely to have occurred by chance or by other potential cancer risk factors that were not included in the analysis, including genetics, lifestyle factors, residential and occupational history, or past exposure to harmful environmental contaminants.
Conclusion 2	Without real-time air monitoring data, PA DOH cannot determine the levels of EtO that people inhaled or are inhaling and the associated human health risks. Available modeling data are also insufficient to conduct a health effects evaluation.

Limitations	• The cancer data analysis lacks information on other potential causes of cancer such as lifestyle behaviors, occupation, case residence history, genetic predisposition, etc. The PA cancer registry does not collect this information. • Only cancers diagnosed in PA residents are reported to the PA cancer registry. Diagnoses made after the individual moved out of state are not included in the registry. Likewise, diagnoses made in people who have recently moved into the Commonwealth (with exposures happening elsewhere) are included in the registry. • **Due to the limitations related to cancer registry data, our cancer analysis cannot determine whether cancer incidences near the B. Braun facility were caused by EtO exposure.** • Historical EtO exposure levels cannot be accounted for or evaluated, particularly when the facility reported notably high EtO emissions.
Recommendations	When advanced technology is available to precisely measure ambient EtO levels, PA DOH recommends that the PA Department of Environmental Protection (PA DEP) or the U.S. Environmental Protection Agency (EPA) or B. Braun perform ambient air monitoring near the EtO-emitting facility and in the surrounding community located downwind from the facility. In the meantime, PA DOH recommends using the most refined dispersion air modeling possible, • to better quantify current and future risks to residents from B. Braun EtO emissions; and, • to confirm the recent actions taken by the facility to reduce emissions and subsequent exposures in the community. PA DOH recommends PA DEP continue to follow-up on the actions taken by the B. Braun facility to reduce EtO emissions.
Next Steps	• PA DOH will post this cancer data review on the PA DOH website available for community members and other interested stakeholders. • PA DOH is available to work with environmental agencies to determine how best to conduct EtO air monitoring to assess human health risks. • PA DOH will evaluate the real-time air monitoring data when available to determine whether the EtO emissions represent a public health concern to people residing near the facility. • PA DOH will continue to respond to community requests to review cancer incidence data in the population surrounding the B. Braun facility.

Public Health Actions	• Since 2018, EPA has been reviewing its Clean Air Act regulations for facilities that release EtO to the outdoor air. • In July 2020, a new emission control system was installed by the facility, which achieved a 99.9% EtO emission reduction, thus reducing the potential exposure and health effects. • In 2022, EPA is planning to issue a proposal on the air toxic rule for EtO commercial sterilizers.
For more information	Please contact PA DOH at 717-787-3350 or by email at Env.health.concern@pa.gov

Background

B. Braun is a German medical and pharmaceutical device company with global operations. B. Braun Medical is headquartered in Bethlehem, PA, and its primary manufacturing facilities are located in Allentown, PA; Irvine, CA; Carrollton, TX; and the Dominican Republic.

B. Braun Site Description and History

The B. Braun Medical facility (the site) is located at 901 Marcon Blvd. in Allentown, Hanover Township, Lehigh County, Pennsylvania. The site is approximately 30 acres surrounded by commercial, residential, and other mixed-use purposes. The Lehigh Valley International Airport and airport tarmac are located in the west and northwest direction from the site. Residential properties such as Hanover Township's Allendale neighborhood are located southwest. Other shopping complexes, residential areas, and commercial centers are located on the east and southeast side of the site (Figure 1). A closer view of only the site is given in Appendix A, Figure A1. This site has been in operation since 1984 and manufactures, prepares, and sterilizes medical devices such as valves, adapters, piercing devices, stopcocks, infusion pumps and systems, syringes, balloon catheters, fluid administration systems, interventional products, and other safety products. It is one of the largest employers in the Lehigh Valley, with approximately 2,000 workers.

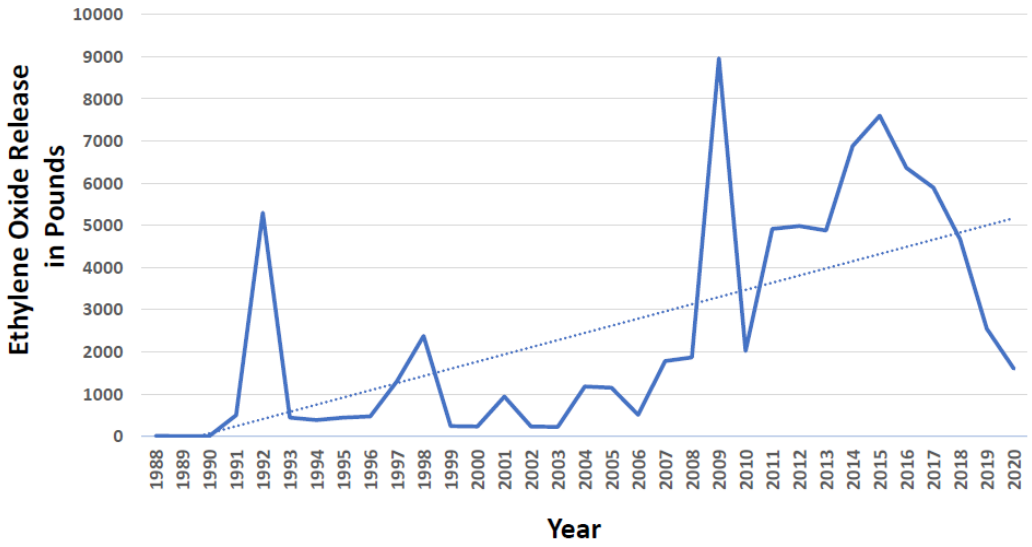
Figure 1: Aerial View of B. Braun and the Surrounding Communities

Toxic Release Inventory (TRI)

B. Braun reports its emissions to the EPA's Toxic Release Inventory (TRI). The EPA's TRI tracks the release of certain toxic chemicals into the air or water by industrial facilities. TRI emissions data are self-reported by the facilities, and there are limitations to its interpretation. However, TRI data helps identify site-related pollutants and inform communities about possible exposure to harmful chemicals. Based on the TRI data for the site, ethylene oxide (EtO) emissions fluctuated but displayed an overall increasing trend from the year 1988 to 2020 (Figure 2). EtO emissions peaked over a seven-year period to near or above 5,000 pounds and ranged from one (1990) to 8,960 (2009) pounds per year. In addition, the reported TRI data (1988 to 2020) for B. Braun did not account for fugitive emissions prior to 2018. The fugitive emission contribution in 2019 and 2020 were 240 pounds, which is approximately 10% and 15%, respectively, of total emissions in those years. (Note: A new emission control system was installed in July 2020).

Fugitive emissions are irregular releases from sterilization chambers, aeration rooms, leaking valves, vents, and other activities. Fugitive emissions vary with wind speed and atmospheric and ground moisture content. According to EPA's recent emission investigations at other EtO release facilities, about 70% of EtO emissions are from unregulated fugitive sources. Currently, states like Illinois have proposed that their facilities limit EtO emissions to 110 pounds per year and fugitive emissions to under 60 pounds per year [EPA 2021]. EPA is currently collecting emissions and emission control data from the site and will use this information to craft a proposed rule revision to better address public health risks from commercial sterilizer EtO emissions [EPA 2021a].

Figure 2: Toxics Release Inventory by B.Braun in Allentown for Ethylene Oxide Air Emissions (1988-2020)



Source: Toxic Release Inventory (TRI), available at https://enviro.epa.gov/facts/tri/ef-facilities/#/Chemical/18018BRRNM824TW

On January 31st, 2020, PA DEP issued a plan approval to B. Braun Medical Inc. to construct and operate enhanced emission control equipment to reduce EtO emissions associated with B. Braun's medical instrument apparatus sterilization operations. The new emission control system installed in July 2020 achieved a 99.9% estimated EtO emission reduction, including the back vent, which is one of the potential sources of fugitive emissions. [Mark J Wejkszner, email communication, June 7th, 2021].

Demographics

We examined the 2010 U.S. Census demographic statistics surrounding the site (within a 2-mile radius) to identify the total population, population distribution, population mobility, and sensitive populations such as young children under six years of age (Appendix A: Figures A2 and A3).

The 2010 U.S. Census estimated that about 4,700 people lived within a 1-mile radius of the site, and about 38,100 people lived within a 2-mile radius from the site. According to the Census, within a 2-mile radius, approximately 8,200 individuals (21%) were adults aged 18-34 years, 6,500 (17%) were children aged 3-17 years, 7,600 (20%) were females aged 15 to 44 years of age, 6,900 (18%) were adults aged 65 and older, and 3% were aged 2 and younger (Appendix A: Figure A3). There was a minimal increase (+1%) in the total population and a slight increase in the population of children (+13% for children aged 2 and younger and +10% for children aged 3 - 17 years) from 2000 to 2010. The population increased from 2000 to 2010 for Black and "other race," and for those with Hispanic ethnicity. The majority of

residents were White (78%), followed by Black (7%), some other race (5%), Asian (2%), and American Indian, Alaskan Native, Native Hawaiian, and Other Pacific Islander (1%). There are three daycare centers within a mile radius and twenty daycare centers within a 2-mile radius of the site (Appendix A: Figure A3). These daycare centers ranged in size and can accommodate from 6 to 119 children per center.

We also reviewed social vulnerability index (SVI) and EPA's 2020 environmental justice (EJ) indicators near the site. SVI is an indicator of a community's readiness and ability to respond to natural or man-made disasters. Various indicators such as socioeconomic status, household composition, race, and housing are combined to calculate this index. The higher the ranking of a community's total social vulnerability, the less likely it is to have resources in place to effectively respond to a disaster. ATSDR estimates showed that about 17,500 people living in communities within a 2-mile radius of the site were in the highest social vulnerability class (Appendix A: Figure A4). Communities most impacted by environmental harms and risks are typically referred to as "EJ communities" or, "overburdened communities". Environmental risk-burdened communities have additional factors (e.g., lack of access to healthy foods, open space, and health care) that can impact health along with environmental contaminant exposures. These factors can affect community health outcomes. EPA's EJ screen tool (EPA 2020) combines publicly available environmental and demographic indicators to identify communities that might be disproportionately burdened by environmental hazards. It is important to note that this EJ screening tool examines only some of the relevant issues related to EJ and there is uncertainty in the evaluation of the data. EJ screening does not analyze data on every environmental and demographic factor that may be important to a specific location. For the population within a 2-mile radius from the site, all the environmental indicators (except ozone and $PM_{2.5}$ in Pennsylvania) and the demographic indicators (except population over 64 years) were above the 50^{th} percentile, meaning the observed EJ indices are relatively uncommon in other communities (communities in Pennsylvania, the EPA Region 3, and the USA).

Community Health Concerns

Bethlehem residents, Lehigh Valley residents, and their elected officials raised concerns about cancer risks associated with the site's EtO emissions. The U.S. House of Representative Susan Wild requested ATSDR conduct a health consultation evaluating the potential health effects from exposure to EtO emissions. In a news report, residents expressed concerns about high numbers of cancer cases, such as brain, prostate, lung, breast, and stomach cancers, in their neighborhood [Morning Call, 2019]. On May 4^{th}, 2021, residents from Allentown, Bethlehem, Coopersburg, Kunkletown, Northampton, and Whitehall Township filed a lawsuit against B. Braun for causing cancers in their neighborhood from decades-long releases of cancer-causing EtO gas in the air [Morning Call, 2021].

Ethylene Oxide (EtO)

Ethylene oxide (EtO) is not a naturally occurring contaminant, but commercially generated from petroleum or natural gas through ethylene oxidation using silver oxide as a catalyst. It is a highly volatile organic colorless gas with a sweet odor. It is highly reactive with nucleophilic substances such as water, alcohols, halides, amines, and sulfhydryl compounds and readily absorbed and distributed in the human body following exposure. No data are available on the fate of EtO in soil [ATSDR 2020].

Ethylene oxide is used in the production of synthetic fibers (e.g., upholstery, carpet), plastics, PVC pipes, and cosmetics and, therefore, can be found in indoor air. It is also used to sterilize medical equipment, as is the case with B. Braun. People can also be exposed to very small amounts from sterilized packaged foods, spices, and cigarette smoke [ATSDR 2020a]. Ethylene oxide has been measured at low levels across the U.S., so people are regularly exposed to small amounts of EtO in air. People living near industrial facilities that release EtO may be exposed to higher levels of EtO than normal background levels. Occupational exposures can occur in worksites that produce or use EtO, including sterilization facilities and hospitals.

Human and animal studies show that EtO can be hazardous to human health as it is easily distributed in the biological system. Short-term health effects such as respiratory irritation, shortness of breath, headache, nausea, vomiting, and diarrhea have been reported in workers exposed to very high concentrations (470,000 $\mu g/m^3$) [NRC 2010].

Long-term low-level exposures to EtO may cause cancer, reproductive effects, genetic changes, and damage to the nervous system. Epidemiological studies have observed a possible association between occupational EtO exposure and cancer risk [ATSDR 2020].

Studies in the U.S. have identified EtO exposure and macromolecule changes (biological indicators) such as hemoglobin adducts, sister chromatid exchanges, and other hematological effects in humans [OEHHA 1999]. Statistically significant decreases in hematocrit and hemoglobin levels were observed in female hospital workers with higher exposure (170 ppb or 300 $\mu g/m^3$) compared to workers with lower exposure (80 ppb or 145 $\mu g/m^3$). Also, a statistically significant increase in lymphocytes and a significant decrease in neutrophils was observed in high-exposure workers compared to controls [Schulte et al., 1995]. Hemoglobin adduct formation is also correlated with the smoking status and the genotype of individuals in the population exposed to EtO via conversion of ethylene found in cigarette smoke [Kolman et al., 2002].

Regulatory History and Ambient Air Ethylene Oxide Concentrations

The U.S. Department of Health and Human Services and the International Agency for Research on Cancer have characterized EtO as a carcinogen to humans [ATSDR 2020a]. The EPA has characterized

EtO as a human carcinogen that has a mutagenic mode of action, meaning it can change the DNA in a cell [EPA 2016]. The National Institute for Occupational Safety and Health studied EtO exposures in sterilizer workers and observed a correlation between EtO exposure and increased risk of developing blood cancers among men and breast cancers among women [Steenland et al., 2003; Steenland et al., 2004]. This human study prompted EPA to revise EtO's classification from probable human carcinogen to human carcinogen [EPA 2005]. In December 2016, EPA updated the new EtO inhalation unit risk value from 0.0001 per $\mu g/m^3$ to 0.003 per $\mu g/m^3$, a 30-fold increase in cancer potency [EPA 2016].

The primary industrial sources of community exposure to EtO are emissions from chemical plants, commercial sterilization operations, and medical facilities. Based on the EPA's EtO ambient air monitoring data (2018-2019) in multiple locations (18 sites) around the U.S. (in nine states) away from known sources of EtO, ambient air concentrations raged from 0.18 to 0.39 $\mu g/m^3$, and the national average was 0.29 $\mu g/m^3$ [EPA 2021b]. **However, EPA was uncertain about the methodology used in measuring low levels of EtO.** Using EPA's 2021 EtO ambient air monitoring data collected from a greater number of locations (41 sites) across the U.S. (16 states) away from known sources of EtO, PA DOH calculated average EtO background concentrations. The concentrations ranged from 0.05 to 0.4 $\mu g/m^3$, and the average was 0.17 $\mu g/m^3$ [EPA 2021c]. However, EPA acknowledges uncertainty in the accuracy of the measured background EtO concentrations. EPA found that SUMMA canisters that quantify EtO in ambient air using the standard analytical method (Compendium of Methods for the Determination of Toxic Organic Compounds in Ambient Air, Method TO-15; or just "TO-15") resulted in a low-level positive bias for some canisters. Since this positive bias, or artifactual detection, is near the method detection limit and within the range reported in areas without known EtO sources, the actual background concentrations of EtO in ambient air are uncertain [EPA 2021]. The EPA is currently investigating this issue by canister batch and manufacturer. Although the current monitoring technology is less accurate in measuring low levels of EtO in ambient air, EPA has high confidence in EtO monitoring results in communities located immediately downwind of EtO emission facilities [EPA 2021d]. Hence, to better characterize emissions from the site, when feasible, real-time ambient air monitoring near the site and in the community located downwind from the site is needed, to identify/or reduce potential EtO emissions and to evaluate human health risks.

Since there is a lack of ambient air monitoring data near the site, PA DOH assessed only the cancer incidence rates of the population living within a 2-mile radius from the site. This is discussed in the next section.

Health Outcome Data Evaluation

As mentioned in the background, the B. Braun Allentown facility has been operating since 1984. For PA DOH's health outcome data evaluation, we looked at the existing cancer registry data from 1985 to 2017 to evaluate cancer incidence patterns for the three time-periods (1985-1994, 1995-2004 and

2005-2017) observed in the community near the B. Braun facility. The cancer data used for the last time-period was for 13 years compared to the other two periods which were for 10 years each. Instead of creating a new time-period for the last 3 years, we combined it with the last time-period. This cancer surveillance data analysis is a descriptive review of cancer incidence near the site and not a research study on evidence that potential exposure to EtO (or any other environmental exposure) has resulted in higher or lower cancer risk.

Cancer Registry Data Review

Cancer is a common disease with many risk factors (genetic, environmental, and behavioral) and long-latency (time gap between initial exposure time and diagnosis or appearance of signs and symptoms) period. For many cancer types, it may take decades for cancer to develop and be diagnosed. People also migrate from one area to another, and therefore it becomes challenging to find the source of exposure that may have caused a particular type of cancer. The Pennsylvania cancer registry does not collect information on the above-mentioned risk factors. Cancer investigations are complex as investigators are aware that there are multiple risk factors involved, incomplete data or missing data on risk factors, no data on individual exposures nor on residential history of the cancer case. Determining the validity of an association between an environmental agent and the development of cancer is difficult, as behavioral (e.g., nutrition, physical activity, and substance use), genetic (e.g., inherited mutations, hormones, and immune conditions), and environmental (e.g., chemicals, radiation, pathogens, and other contaminants) factors interact and affect cancer incidence. As a result, a cancer analysis may provide an overall understanding of a community's health status but cannot provide information on the causation of cancers. Our health outcome analysis using cancer registry data provides information on whether more cases of particular cancer have occurred in the community near the B. Braun facility than in the comparison area. Even if a particular cancer is occurring at a statistically higher rate than expected, the finding could have occurred by chance or be related to other potential cancer risk factors that were not included in the analyses.

The PA DOH selected adult female breast cancer, adult male and female lymphohematopoietic cancers (blood/lymph), and all childhood cancers for the analysis. These cancer types were selected due to their possible association with EtO exposure from scientific studies, though mostly in an occupational setting [Jinot et al., 2018; Steenland et al., 2003; Steenland et al., 2004]. Cancer cases were grouped into adult female breast cancer, adult lymphohematopoietic cancers, and all childhood cancers (anyone diagnosed before 20 years of age with leukemia, brain tumors, lymphomas, Wilms tumor, bone and soft tissue cancer, and other pediatric cancers). Cancer records were divided into three time-periods based on the time of diagnoses: 1985-1994, 1995-2004, and 2005-2017 for each cancer category defined above to identify any trends in cancer incidence rates.

The PA DOH used the traditional statistical method, age-adjusted standardized incidence ratios (SIRs), to calculate cancer incidence rates within a 2-mile radius surrounding the site. The SIR calculation involved comparing the observed number of cancer cases to the number of cases that would be expected, i.e., whether the community experienced the same cancer rate as a larger comparison area (the cancer rate outside of a 2-mile of site radius within Lehigh and Northampton Counties). The observed number of cases was divided by the expected number of cases within a 2-mile radius from the site. This ratio of observed over expected is called a standardized incidence ratio (SIR). A ratio greater than 1.0 indicates that more cases occurred than expected, and a ratio of less than 1.0 indicates that fewer cases occurred than expected. For example, a ratio of 1.5 means the number of observed cancer cases was 50% higher than the expected number, and a ratio of 0.9 means 10% fewer than the expected number. The SIR is considered statistically higher or lower if the 95% confidence interval (CI) does not include 1.0. A statistically higher or lower SIR means the observed SIR is less likely to have occurred by chance, though chance or other risk factor(s) cannot be ruled out. The CI helps to determine the precision of the SIR estimate. The narrower the CI, the greater confidence one has in the SIR estimate. Adult and childhood cancer incidence rates are discussed below.

All cancer cases within a 2-mile radius were geocoded using ArcGIS. This was done to confirm that all the cancer cases were within the geographical area of 2-miles from the site. At the time of this cancer data review, geocoded cancer data was available through calendar year 2017. Census data for 1990, 2000, and 2010 were downloaded from IPUMS NHGIS, University of Minnesota. Census crosswalks were used to link 1990, 2000, and 2010 census blocks.

Adult Cancer Incidence Rates

Adult lymphohematopoietic (including non-Hodgkin lymphoma, myeloma, and lymphocytic leukemia) and female breast cancer incidences were analyzed for three time-periods: 1985-1994, 1995-2004, and 2005-2017. Male lymphohematopoietic cancer incidence rates for time-periods 1985-1994 and 1995-2004 were higher in the 2 miles radius than in the reference area, but these differences were not statistically higher (SIR: 1.07, 95% CI: 0.84-1.35, and SIR: 1.11, 95% CI: 0.90-1.35, respectively, Table 1). For the time-period 2005-2017, the male lymphohematopoietic cancer incidence rate was statistically lower (17%) than the reference area (SIR: 0.83, CI: 0.69-0.99). Female lymphohematopoietic cancer incidence rates for all three time-periods 1985-1994, 1995-2004, and 2005-2017 were higher (9%, 11%, and 2%, respectively) than the reference area, but were not statistically higher (SIR: 1.09, 95% CI: 0.85-1.38, SIR: 1.11, 95% CI: 0.89-1.35, and SIR: 1.02, 95% CI: 0.85-1.21 respectively).

The female breast cancer incidence rate for the time-period 1995-2004 was higher (6%) than the reference area but was not statistically higher (SIR: 1.06, 95% CI: 0.96-1.16). For the remaining two time-periods 1985-1994 and 2005-2017, the incidence rates were lower (6% and 5%, respectively) than

the reference area but were not statistically lower (SIR: 0.94, 95% CI: 0.85-1.04 and SIR: 0.95, 95% CI: 0.87-1.03 respectively).

Childhood Cancer Incidence Rates

The childhood cancers included in this review were leukemia, brain tumors, lymphomas, Wilms tumor, and bone and soft tissue cancer for anyone diagnosed before 20 years of age. Childhood cancer incidences from 1985-2017 were analyzed for three time-periods (1985-1994, 1995-2004, and 2005-2017). The male childhood cancer incidence rate for time-period 1985-1994 was lower (17%) than the reference area (SIR: 0.83, CI: 0.38-1.58) but not statistically lower (Table 1). For time-periods 1995-2004 and 2005-2017, the cancer incidence rates were higher (9% and 11%, respectively) than the reference area, although they were not statistically higher (SIR: 1.09, 95% CI: 0.52-2.01 and SIR: 1.11, 95% CI: 0.65-1.78 respectively). The female childhood cancer incidence rates for time-periods 1985-1994 and 2005-2017 were ***statistically*** higher (88% and 84% respectively) than the reference area (SIR: 1.88, 95% CI: 1.01-3.22 and SIR: 1.84, 95% CI: 1.19-2.71 respectively). For time-period 1995-2004, the female childhood cancer incidence rates were lower (2%) than the reference area but were not statistically lower (SIR: 0.98, 95% CI: 0.42-1.93).

However, it should be noted that these childhood cancer comparisons are based on a very small number of cancer cases (please see Table 1), which increases the uncertainty of the estimates and makes interpretation of the confidence intervals necessary. The confidence intervals for the SIRs reflecting the higher female childhood cancer incidence rates were wide (indicating statistical imprecision or less confidence in the SIR estimate) and were very nearly crossing the value 1.0. In addition, as mentioned earlier, the cancer data analysis lacks information on other potential causes of cancer such as lifestyle behaviors, occupation, genetic predisposition, etc. Therefore, these analyses cannot indicate whether cancer incidence rates near the B. Braun facility are caused by EtO exposure. Only cancers diagnosed in PA residents are reported to the PA cancer registry.

Hence, based on the SIR analysis for this site, there were no consistent increasing or decreasing trends or patterns in cancer incidence rates for all three time-periods (1985-1994, 1995-2004, and 2005-2017) near the site for any of the cancer types selected for this analysis. Additional studies with larger exposed populations would lend greater statistical power to cancer outcome analysis to better identify whether rare cancers occur more frequently in an exposed population than an unexposed population.

Table 1: Cancer Incidence Rates of Adults and Children near B. Braun facility

Adult Lymphohematopoietic Cancers						
Statistics	**1985 – 1994**		**1995 - 2004**		**2005 - 2017**	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
Observed	72	71	99	94	121	126
Expected	67.2	65.0	89.5	85.1	145.3	123.9
SIR	1.07	1.09	1.11	1.11	***0.83***	1.02
95% CI	0.84 - 1.35	0.85 - 1.38	0.9 - 1.35	0.89 - 1.35	***0.69 - 0.99***	0.85 - 1.21
Female Breast Cancer						
Statistics	**1985 – 1994**		**1995 - 2004**		**2005 - 2017**	
Observed	366		451		521	
Expected	388.3		425.5		550.4	
SIR	0.94		1.06		0.95	
95% CI	0.85 - 1.04		0.96 - 1.16		0.87 - 1.03	
All Childhood Cancers (Diagnosed before 20 years of age with leukemia, brain tumors, lymphomas, Wilms tumor, bone and soft tissue cancer, and other pediatric cancers)						
Statistics	**1985 – 1994**		**1995 - 2004**		**2005 - 2017**	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
Observed	9	13	10	8	17	25
Expected	10.8	6.9	9.2	8.2	15.3	13.6
SIR	0.83	**1.88**	1.09	0.98	1.11	**1.84**
95% CI	0.38 - 1.58	**1.01 - 3.22**	0.52 - 2.01	0.42 - 1.93	0.65 - 1.78	**1.19 - 2.71**

SIR = Standardized Incidence Ratio; 95% CI = 95% Confidence Interval; Numbers bolded and in italics were statistically lower than the reference area, and numbers that were only bolded were statistically higher than the reference area.

As noted, this cancer surveillance data analysis is a descriptive review of cancer incidence rates near the site and not a research study on evidence that potential exposure to EtO (or any other environmental exposure) has resulted in higher or lower cancer risk.

Conclusions

PA DOH reached the following two conclusions:

Conclusion 1

Age-adjusted cancer incidence rates, when analyzed by time-period and gender, do not present a consistent pattern. Unstable cancer rates were found and are most likely due to the small sample size (cancer rates based on the population within a 2-mile radius). The cancer rates observed in our analysis are not consistent with cancer patterns often associated with environmental exposure.

Basis for conclusion

Our cancer analysis within a 2-mile radius of the site revealed no consistent pattern for adult lymphohematopoietic and female breast cancer rates between 1985-2017:

- Male lymphohematopoietic cancer rates were higher (7% and 11% respectively) between 1985-1994 and 1995-2004, compared to the reference area but none were statistically higher. For the time-period 2005-2017, male lymphohematopoietic cancers were statistically lower (17%).
- Female lymphohematopoietic cancers were higher (9%, 11%, and 2% respectively) for all three time-periods, but none were statistically higher.
- Female breast cancer rates were lower (6%) between 1985-1994, higher (6%) between 1995-2004, and lower (5%) between 2005-2017 but none of these rates were statistically higher or lower.

We observed similarly inconsistent patterns in childhood cancer rates:

- Male childhood cancers within 2 miles of the facility were lower (17%) than the reference area between 1985-1994 and higher (9% and 11% respectively) between 1995-2004 and 2005-2017, but none of these rates were statistically lower or higher.
- Female childhood cancers were statistically higher (88% and 84% respectively) than the reference area from 1985-1994 and 2005-2017. However, from 1995-2004, female childhood cancers were slightly lower (2%) than the reference area and were not statistically lower.

There is no consistent pattern of cancer incidence rates among adults or children living within a 2-mile radius of the B. Braun facility relative to adults and children living outside the 2-mile radius. Difference in cancer rates indicate that the finding is more likely to have occurred by chance or by other potential cancer risk factors that were not included in the analyses.

Conclusion 2

Without real-time air monitoring data, PA DOH cannot determine the levels of EtO that people inhaled or are inhaling and the associated human health risks. Available modeling data are also insufficient to conduct a health effects evaluation.

Limitations

- The cancer data analysis lacks information on other potential causes of cancer such as lifestyle behaviors, occupation, case residence history, genetic predisposition, etc. The PA cancer registry does not collect this information.
- Only cancers diagnosed in PA residents are reported to the PA cancer registry. Diagnoses made after the individual moved out of state are not included in the registry. Likewise, diagnoses made in people who have recently moved into the Commonwealth (with exposures happening elsewhere) are included in the registry.
- **Due to the limitation related to cancer registry data, our cancer analysis cannot determine whether cancer incidence rates near the B. Braun facility were caused by EtO exposure.**

- Historical EtO exposure levels cannot be accounted for or evaluated, particularly when the facility reported notably high EtO emissions.

Recommendations

When advanced technology is available to precisely measure ambient air EtO levels, PA DOH recommends that the PA DEP or the EPA or B. Braun perform ambient air monitoring near EtO-emitting facility and in the surrounding community located downwind from the facility. In the meantime, PA DOH recommends using the most refined dispersion air modeling possible,

- to better quantify current and future risks to residents from B. Braun EtO emissions; and,
- to confirm the recent actions taken by the facility to reduce emissions and subsequent exposures in the community.

PA DOH recommends PA DEP continue to follow-up on the actions taken by the B. Braun facility to reduce EtO emissions.

Next Steps

- PA DOH will post this cancer data review on the PA DOH website available for community members and other interested stakeholders.
- PA DOH is available to work with environmental agencies to determine how best to conduct EtO air monitoring to assess human health risks.
- PA DOH will evaluate the real-time air monitoring data when available to determine whether the EtO emissions represent a public health concern to the people residing near the facility.
- PA DOH will continue to respond to community requests to review cancer incidence data in the population surrounding the B. Braun facility.

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Appendix A

Figures

Figure A1: Facility Location Map

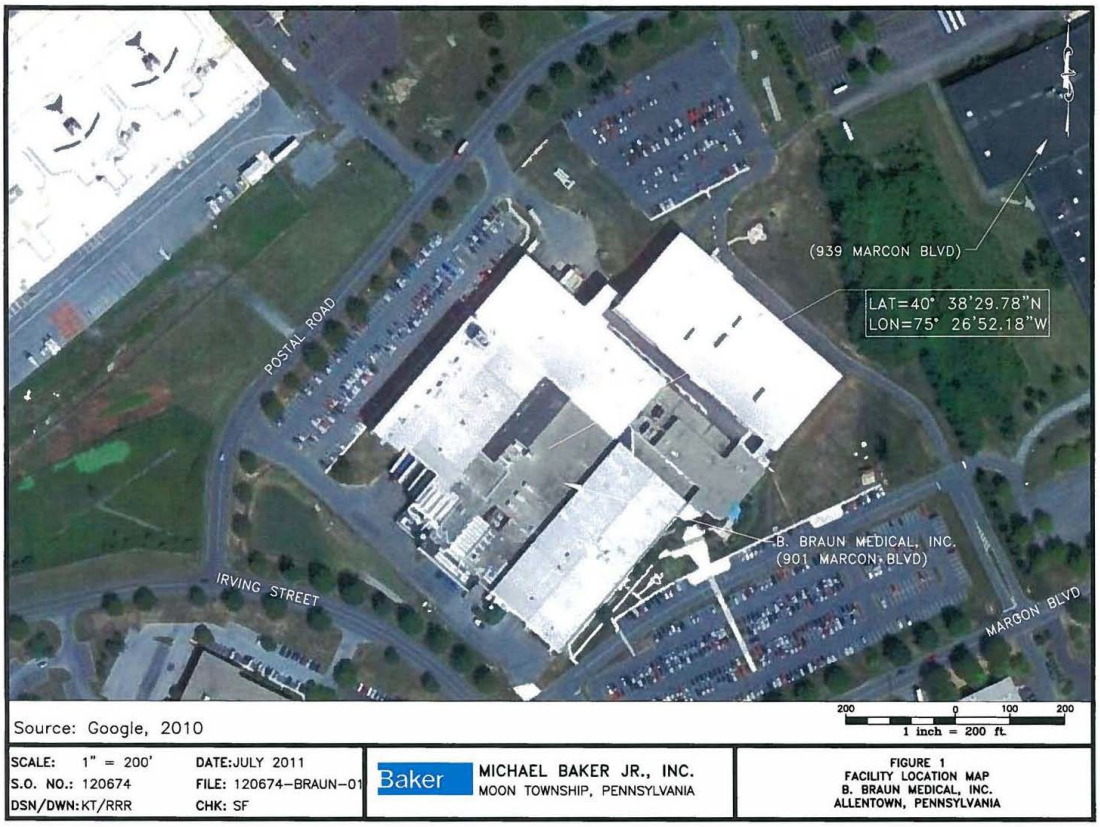
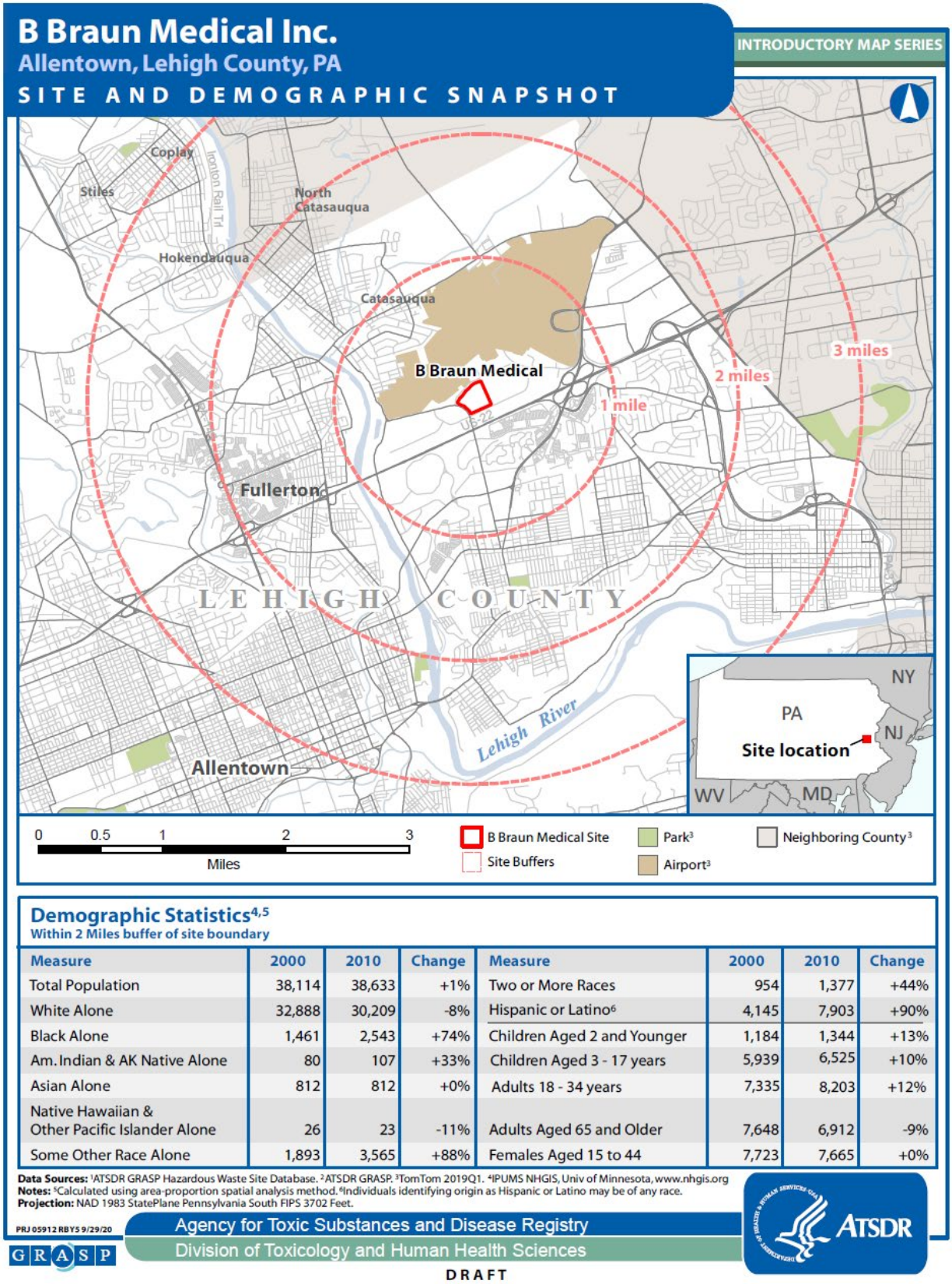


Figure A2: Site and Demographics



Demographic Statistics[4,5]

Within 2 Miles buffer of site boundary

Measure	2000	2010	Change	Measure	2000	2010	Change
Total Population	38,114	38,633	+1%	Two or More Races	954	1,377	+44%
White Alone	32,888	30,209	-8%	Hispanic or Latino[6]	4,145	7,903	+90%
Black Alone	1,461	2,543	+74%	Children Aged 2 and Younger	1,184	1,344	+13%
Am. Indian & AK Native Alone	80	107	+33%	Children Aged 3 - 17 years	5,939	6,525	+10%
Asian Alone	812	812	+0%	Adults 18 - 34 years	7,335	8,203	+12%
Native Hawaiian & Other Pacific Islander Alone	26	23	-11%	Adults Aged 65 and Older	7,648	6,912	-9%
Some Other Race Alone	1,893	3,565	+88%	Females Aged 15 to 44	7,723	7,665	+0%

Data Sources: [1]ATSDR GRASP Hazardous Waste Site Database. [2]ATSDR GRASP. [3]TomTom 2019Q1. [4]IPUMS NHGIS, Univ of Minnesota, www.nhgis.org
Notes: [5]Calculated using area-proportion spatial analysis method. [6]Individuals identifying origin as Hispanic or Latino may be of any race.
Projection: NAD 1983 StatePlane Pennsylvania South FIPS 3702 Feet.

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Figure A3: Sensitive Population

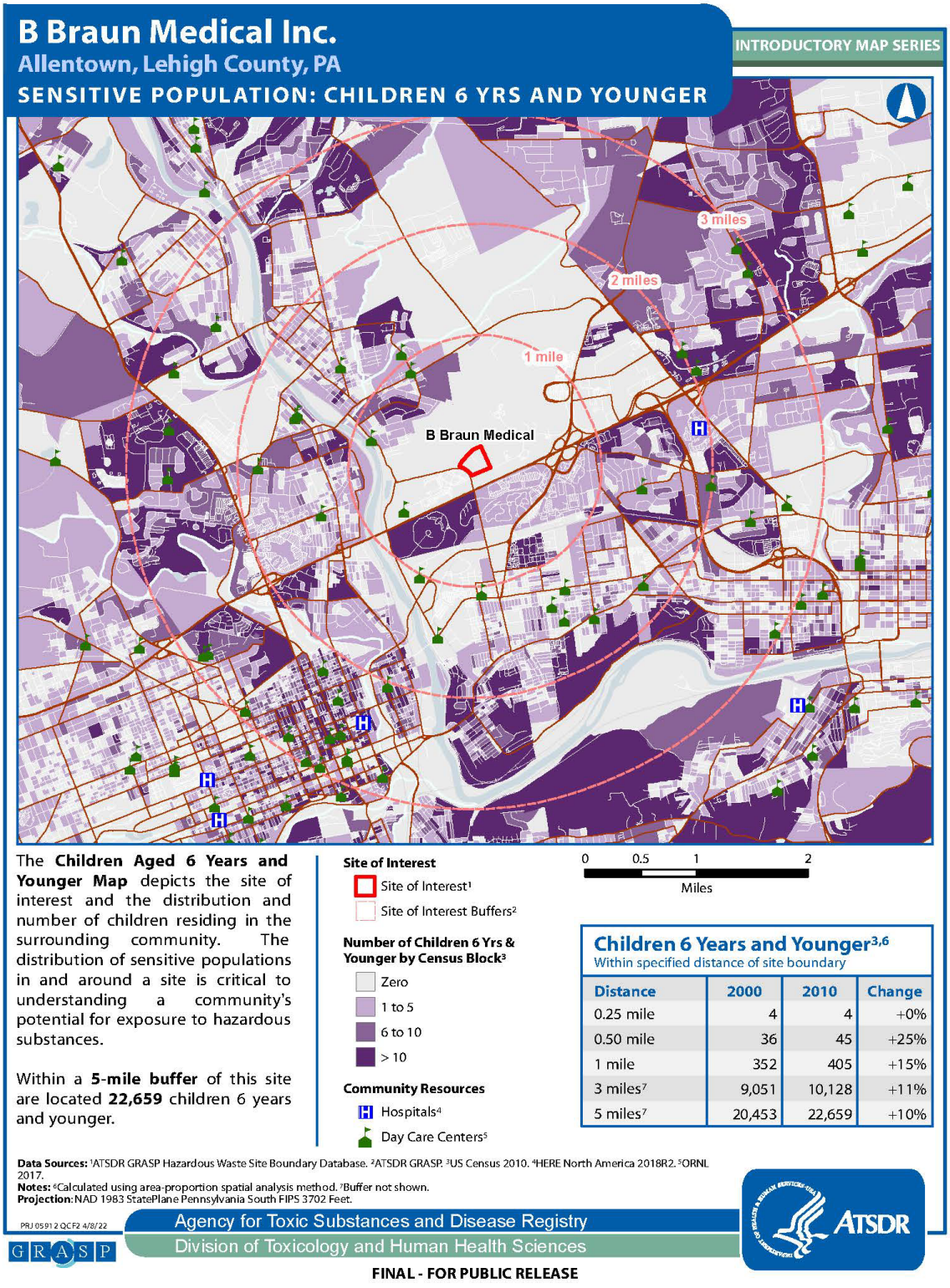

Figure A4: Social Vulnerability Index