



Center for Environmental Health Center for Community Health

Health Consultation Health Outcomes Review: Adverse Birth Outcomes and Cancer Incidence

Village of Liberty Sullivan County, New York

December 28, 2012

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&
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Under a cooperative agreement with
The U.S. Department of Health & Human Services
Agency for Toxic Substances and Disease Registry
Public Health Service
Atlanta, Georgia

This report was partially supported by funds
from the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA)
provided to the New York State Department of Health under a cooperative agreement
from the Agency for Toxic Substances and Disease Registry (ATSDR)
U.S. Department of Health and Human Services.

This report was produced independently by NYSDOH and was not reviewed by ATSDR.

SUMMARY

A health outcomes review was conducted for the Village of Liberty because of concerns about health effects from methyl tert-butyl ether (MTBE) in the water supply system. A health outcomes review examines a particular group of people as a whole to see how it compares to a group not living in the area of concern. It cannot link an environmental exposure to a specific health effect and it cannot tell us anything about individual health problems.

This health review covered the time period between 1979 and 2005 and focused on the outcomes of low birthweight, premature births, birth defects and cancer for the population exposed in the past to MTBE. The purpose of this review was to compare the number of these health outcomes for people who lived in Liberty to people who lived in the rest of the state. This comparison showed nothing unusual for any of the birth outcomes or cancer in general. Looking specifically at 17 types of cancer in males and 19 types in females, two statistically significant elevations were noted:

- A higher than expected number (65 vs. 46) of lung and bronchial cancers among women 65-74. This type of cancer is not associated with exposure to MTBE in animals, but is associated with smoking history. A majority of the women who were diagnosed with lung cancer whose smoking history was known were current or former smokers.
- A higher than expected number (18 vs. 10) of leukemias diagnosed among men between 1990 and 2003. We do not know whether MTBE can cause cancer in humans, but leukemia is one type of cancer associated with MTBE exposure in animals. Although this is not a cause and effect link and may, in fact, be due to chance or other possible exposures, we recognize this may raise concerns among men and their families. Individuals who are concerned are encouraged to share this information with their health care providers.

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EXECUTIVE SUMMARY

Health Outcomes Review of Adverse Birth Outcomes and Cancer Incidence Village of Liberty, Sullivan County, New York

Background

The New York State Department of Health (NYS DOH) conducted this health outcomes review because of concerns about environmental health issues related to contamination detected in the Village of Liberty water supply system, Sullivan County, New York. This type of review looks at health outcomes among the population of a specific geographic area and provides residents with information about the numbers of outcomes in their area compared with expected numbers based on statewide data. This type of review cannot link cause (exposure) and effect (health outcome) and cannot relate an individual person's health problem to a specific environmental exposure.

In December 1992, contamination of water from the Village of Liberty's Elm Street well by a gasoline additive called methyl tert-butyl ether (MTBE) was discovered at levels that exceeded the NYS DOH drinking water standard in effect at that time. The Elm Street well was the primary source of water for the Village of Liberty and also served the Town of Liberty's Ferndale and Stevensville water districts. Approximately 4,000 people in these water districts were potentially exposed to MTBE at levels above the applicable NYS DOH drinking water standard for an undetermined amount of time, possibly from as early as 1979, when MTBE was first used as a gasoline additive, to January 1993 when the distribution system was flushed and the well was temporarily taken out of service. Village residents were potentially exposed to levels above the applicable standard again for the month of November 1993. Water testing data from 2004 to spring 2011 show no elevations of MTBE. (People may have also been exposed to MTBE in other ways, primarily while pumping gas.)

There are no data on the effects in people of drinking water contaminated with MTBE. Animal studies have shown that drinking MTBE is associated with a variety of effects in rodents, including gastrointestinal irritation, liver and kidney damage, nervous system effects, testicular cancer, leukemia, and lymphoma. Animal studies have also shown that breathing high levels of MTBE for long periods is associated with kidney and liver cancer in rodents. It is not known, however, whether MTBE can cause cancer in humans. (ATSDR, 1997; USDHHS, NTP 1998) This health outcomes review focuses on adverse birth outcomes, including low birth weight, prematurity, and birth defects; and cancer, including 17 types in males and 19 types in females. This type of review is feasible because NYS DOH collects comprehensive data on these health outcomes for all NYS residents.

Methods

The boundaries of the birth outcomes review study area were selected by identifying the boundaries of the water districts served by the Elm Street well. For the birth outcomes analyses, separate exposure areas and timeframes were developed to reflect the history of contamination affecting the Village of Liberty, and Town of Liberty's Ferndale and Stevensville water districts. Five exposure groups were developed based on the available data about MTBE levels in the Elm Street well. While there is no information about MTBE levels prior to 1990 (when low-level MTBE contamination was first detected), residents of all three water districts are assumed to have been potentially exposed to increasing levels of MTBE from 1979 through 1992 for the purpose of potential exposure assignments for this study.

From 1993 to 1998, sampling shows that levels of MTBE were generally lower, but varying, for the Village of Liberty. No measurable MTBE exposures from public water occurred for the Village of Liberty from 1999 to 2005, and for Ferndale and Stevensville from 1993 to 2005. (The current investigation uses health outcomes data through 2005.) (See later sections of this report for a full description of the five exposure groups and details about MTBE sampling.)

Because contamination may have begun as early as 1979, we selected 1979 as the first year of the study time frame for birth weight outcomes. Low birth weight, prematurity, two growth restriction categories (term low birth weight and small for gestational age), and male to female sex ratio were examined for the years 1979-2005. 2005 was the most recent year of available data when the study began. All reportable birth defects were evaluated for 1983-2004, since 1983 is the first year of birth defect data and 2004 was the most recent year of available data from the NYS Congenital Malformations Registry when the study began. For the birth outcomes low birth weight, prematurity, and growth restriction, and birth defects, Poisson regression modeling was used to evaluate the risk associated with mother's residence in the study area at the time of the birth. The regression models take into account each mother's age, education, race, number of previous live births, prenatal care, and the baby's gender, and compare rates of outcomes in the Liberty exposure areas to rates in NYS (excluding NYC). These comparisons are presented as rate ratios (RRs). The RR is the rate in the exposure area divided by the rate in NYS (excluding NYC).

NYS DOH reviewed cancer incidence in the study area for the time period 1990-2003. The end year for the cancer study is the most recent period for which cancer reporting was considered complete at the time the study was initiated, and the beginning year was chosen to obtain a sufficient number of diagnoses to see an effect and to allow sufficient latency. The boundaries of the cancer study area were defined as the boundaries of ZIP Codes 12754 and 12768, which contain more than 50% of the population in the three water districts impacted by the Elm Street well. The actual observed numbers of people diagnosed with cancer during 1990-2003, by sex and type of cancer, were counted from the New York State Cancer Registry. The expected numbers of people diagnosed with cancer during these same years, by sex and type of cancer, were calculated based on the age and sex distribution of people living in the study area. The actual numbers were compared to the expected numbers for 17 types of cancer and total cancers among men, and for 19 types of cancer and total cancers among women. These comparisons are presented as standardized incidence ratios (SIRs). The SIR is the number of cases observed divided by the number of cases expected.

Results

When the exposure groups with potential exposure to MTBE from the Elm Street well were combined, no type of adverse birth outcome was statistically significantly elevated. When the exposure groups with potential MTBE exposures were evaluated separately, there were also no statistically significant results. However, these separate analyses did suggest an elevation of risk in the exposure group with the highest potential exposures to MTBE (Group 2, comprising Liberty, Ferndale and Stevensville Water Districts, births in 1986-1993). The rate ratios for this group (comparing outcomes in this group to statewide levels) showed elevations for more conditions than the other exposure groups, and although not statistically significant, these rate ratios were of higher magnitude than in the other MTBE exposure groups. In this highest potential exposure group, the elevation for preterm births (62 observed, 45.6 expected) produced a rate ratio (RR) of 1.24 that was close to being statistically significant (95% confidence interval [CI]: 0.97-1.59). Evaluation of these outcomes using an alternative estimate of

gestational age, provided by the clinician and available on birth certificates, showed no evidence of an elevation, however (data not shown). In this highest potential exposure group, the two adverse birth outcome categories showing the most elevated rate ratios were the categories with the smallest numbers and very low statistical power for detecting an elevation. These categories are “very low birth weight” (RR 1.57, CI: 0.79 - 3.14) and “very preterm” (RR 1.54, CI: 0.93 - 2.55). (These categories would include many of the same births.)

The adverse birth outcome analyses did produce one statistically significant elevation, for term low birth weight, but this elevation occurred in the Liberty Water district from 200 through 2005, when residents were not exposed to elevated levels of MTBE from the Elm Street well. This elevation for term low birth weight was just above the borderline for statistical significance (RR 1.77, CI: 1.00 - 3.11) and was comprised of twelve term low birth weight births compared to approximately six expected.

A total of 66 birth defects were included in the analyses and 65.6 were expected. A variety of defects were represented in the total, with musculoskeletal defects, heart defects and defects of the genitourinary system reported most frequently. There were no statistically significant excesses (or deficits) of birth defects during the period when MTBE exposures are expected to have occurred or in the later, post-MTBE time period. There was nothing unusual noted about the pattern of birth defects.

Overall, the actual number of men diagnosed with cancer was not statistically significantly different from the number expected (344 cases observed; 340 cases expected). Looking at specific types of cancer, a statistically significant excess was found in the number of men diagnosed with leukemia (18 cases observed, 10 cases expected; SIR 1.75, CI: 1.04 - 2.77). As is usually seen with leukemia, the majority of cases were found in people over the age of 65, and the most frequently diagnosed subtypes were acute myelogenous leukemia (AML) and chronic lymphocytic leukemia (CLL). A statistically significant deficit was found in the number of men diagnosed with multiple myeloma (0 cases observed; 4 cases expected). No other specific types of cancer showed a statistically significant excess or deficit.

Overall, the actual number of women diagnosed with cancer was not statistically significantly different from the number expected (369 cases observed, 336 cases expected). Looking at specific types of cancer, a statistically significant excess was found in the number of women with cancer of the lung and bronchus (65 cases observed, 46 cases expected; SIR 1.41, CI: 1.09 - 1.79). No other specific type of cancer showed a statistically significant excess and no specific type of cancer showed a statistically significant deficit.

Studies have shown that MTBE is associated with an increased risk of leukemia in animals; it is not known whether it is associated with an increased risk of leukemia in humans. In the present study, a statistically significant excess number of cases of leukemia was observed among males. The number of females diagnosed with leukemia was close to the number expected. Risk factors for leukemia include Down’s syndrome, other genetic abnormalities, exposures to benzene or high doses of ionizing radiation, certain anti-cancer drugs, smoking, and a high weight at birth. More than half of all cases occur in people over the age of 65. In the study area, two-thirds of the males were diagnosed after age 65. No individual 10-year age group showed a statistically significant excess when examined separately. A majority of the males and females diagnosed with leukemia resided in the Village in areas supplied by the Elm Street Well, as would be expected, based on the population distribution. There was no obvious concentration in any particular area of the Village. Medical records and death certificates showed that a

small number of the males diagnosed with leukemia had known medical or occupational risk factors for leukemia.

In addition to leukemia, cancers associated with MTBE exposure in animals are cancers of the liver, testis, and kidney, and lymphomas. It is not known whether MTBE causes any of these cancers in humans. None of these types of cancers were statistically significantly elevated in the study area. In the present study, a statistically significant excess was found in the number of women diagnosed with cancer of the lung and bronchus. The number of males diagnosed with this cancer was close to expected. This cancer is not associated with MTBE exposure in animals. Cancer of the lung and bronchus is one of the most common cancers among New Yorkers with smoking being the most important cause. Some research studies show that exposure to other people's cigarette smoke, exposure to radon gas, and exposure to asbestos and certain other substances found in the workplace also increase the risk for this cancer. When individual age groups were examined separately, a statistically significant excess for lung cancer was found in females aged 65-74 years. For all other age groups, numbers of cases were close to expected. Residences of the females were found to be scattered throughout the study area with about half of the women residing in the Village. Plotting the residential addresses did not show any evidence of unusual geographic distribution.

Conclusions

In analyses of three exposure groups with potentially differing levels of MTBE exposures, there were some results suggesting elevated risks in the exposure group with the highest potential exposures to MTBE (group 2). In this group, there were rate ratios for more conditions showing elevations, and although not statistically significant, these rate ratios were of higher magnitude than in the other MTBE exposure categories. The one birth outcome that was statistically significantly elevated in this investigation was at the borderline of significance, and it was for term low birth weight births occurring after MTBE exposures from the Elm Street well had ended (RR 1.77, CI: 1.00 - 3.11) (group 4).

Regarding the cancer findings, leukemia is the one type of cancer associated with MTBE exposures in animals that was statistically significantly elevated in this investigation for the years 1990-2003. The elevation was only among men, with 18 cases observed versus 10 cases expected. The lack of an elevation of leukemia diagnoses in the earlier time period, 1980-1989, is consistent with the interpretation that a latency period, or time-lag, produced elevated leukemia incidence only during the more recent time period. The majority of the men diagnosed with leukemia lived in the area supplied by water from the Elm St. well, as would be expected given the population distribution. A small proportion of them had known individual risk factors. The pattern of age at diagnosis for the men with leukemia was not unusual. Given the number of individual types of cancer evaluated, it is possible that this statistically significant elevation occurred by chance. In addition, most cancers, including leukemia, have more than one possible cause, and this study did not have enough information available to identify and evaluate all other possible causes in this population.

This type of review cannot prove a causal link between exposure and a specific health outcome. Similarly, the findings, whether they show statistically significant elevations or not, do not reveal whether any specific health outcome may have been caused by an environmental exposure. The small numbers of outcomes for some rare types of outcomes, which include many types of cancer and birth defects, limit the strength of conclusions that can be drawn from this review.

Because of the shorter latency period for birth outcomes and the multivariate analyses performed to produce birth outcome findings that take account of other risk factors, these findings lend themselves to stronger interpretation than the cancer findings. While some of the low birth weight findings for the exposure group with the highest potential exposures are suggestive of a possible effect of MTBE, the findings were not statistically significant which means no effect was detected.

Recommendations

- We recommend this report be shared with Liberty-area residents. We released a draft version of this report in February 2012 for public comment, providing an opportunity for questions and comments. We sent postcards announcing the report's release to area residents who had expressed interest in the past. This final version of the report contains no changes to the report, with the exception of the addition of a summary of the public comments and responses to comments (Appendix C). This final report will be posted on the NYS DOH public website.
- Although the results of this review are not definitive, it is recommended that the investigation's methods and findings be written as a report for a peer-reviewed publication so that the findings are available to the scientific community as well as other interested stakeholders.
- There was a statistically significant excess of leukemia among men in the time period 1990-2003, and leukemia is one type of cancer associated with MTBE exposure in animals. Although this is not a cause and effect link and may, in fact, be due to chance or other possible exposures, we recognize this may raise concerns among men and their families. For anyone who is concerned, we recommend they share this information with their health care provider and discuss their concerns. Health Department staff is available as a resource to physicians and community members at 518-402-7950.

1.0 INTRODUCTION

This **health outcomes review** was conducted by the New York State Department of Health (NYS DOH) in response to potential environmental exposures and concerns about the health of residents served by the Village of Liberty water supply from 1979 to 1999. This review compared levels of adverse birth outcomes among people served by the Village water supply to levels among NYS residents (excluding New York City). This review also compared levels of cancer in the ZIP Codes containing the Village of Liberty to levels of cancer among NYS residents (excluding NYC).

A health outcomes review uses information from already existing sources, such as birth or cancer records, to compare rates of health outcomes among residents of a specific area to rates in the general statewide population or other appropriate comparison group.

This type of review cannot prove whether there is a causal relationship between specific exposures and health outcomes in a community, nor can it determine the cause of any specific individual's health problems. The findings of this type of review may be used, together with findings from other similar investigations, to suggest hypotheses for more in-depth research studies. The study's findings may also be useful to residents, providing them with specific information about levels of health outcomes in their area.

NYS DOH originally planned to evaluate a more comprehensive list of health outcomes using information from questionnaires mailed out to Village of Liberty residents in June of 2002. However, because fewer than ten percent of households (111 of 1,581 households) returned completed questionnaires, additional evaluation was not possible. The health outcomes review approach uses existing data that provides complete data for the population and its success does not depend on whether people respond to a survey or fill out a questionnaire. A draft version of this report was provided for public comment in February 2012. For this final report, no revisions were made to the text of that earlier report. The only change is the inclusion of a summary of the public comments and our responses, provided in Appendix C.

2.0 BACKGROUND

2.1 Exposure History

Summary: In December 1992, contamination of water from the Village of Liberty's Elm Street well by a gasoline additive called methyl tert-butyl ether (MTBE) was discovered at levels that exceeded the NYS DOH drinking water standard in effect at that time. The Elm Street well was the primary source of water for the Village of Liberty and also served the Town of Liberty's Ferndale and Stevensville water districts. Approximately 4,000 people in these water districts were potentially exposed to MTBE at levels above the applicable NYS DOH drinking water standard for an undetermined amount of time, possibly from as early as 1979, when MTBE was first used as a gasoline additive, to January 1993 when the distribution system was flushed and the well was temporarily taken out of service. Village residents were potentially exposed to levels above the applicable standard again for the month of November 1993. The Stevensville and Ferndale water districts south of the Village received water from the Village of Liberty from 1979 until late 1992. Water testing data from 2004 through spring 2011 show no elevations of MTBE. (People may have also been exposed to MTBE in other ways, primarily while pumping gas.)

From late January 1993 to August 1993, residents of the Village of Liberty were provided with drinking water from alternative water supplies (e.g., water from Revonah Lake, a water tanker and an external tap at the Town of Liberty's water system). From August through November 1993, the Elm Street well was used as the sole source for Village of Liberty residents. After residents were again potentially exposed to levels above the applicable standard during the month of November 1993, Elm Street well water was blended with other Town of Liberty supplies through July 1997, and then was used again as the sole source for the Village through August 1998. In 1998, Lily Pond became the Village's primary source of public water, with the Elm Street well water continuing to be used seasonally as a supplemental source. Water testing data from 2004 through spring 2011 show no elevations in MTBE.

Detailed History: The detailed information below is from the Public Health Assessment (PHA) for the Village of Liberty water supply system - Elm Street well (NYS DOH/ATSDR, 2005). During the process of developing the 2005 Public Health Assessment, the NYS DOH drinking water standard for MTBE was revised to a lower value. The previous NYS DOH standard of 50 micrograms per liter ($\mu\text{g}/\text{L}$) was superseded on December 24, 2003 by the current standard of 10 $\mu\text{g}/\text{L}$.

The Elm Street well was installed and became the Village of Liberty's primary water source around 1960. In December 1992, an engineering firm was hired to operate the village's public water supply. Upon reviewing historical records on the Elm Street well, the firm found laboratory results from a single sample indicating the presence of MTBE in August 1990. Prior to this date, MTBE was not a routinely monitored analyte under the State Sanitary Code for drinking water supplies. A water sample collected from the Elm Street well on December 28, 1992 exceeded the 50 $\mu\text{g}/\text{L}$ maximum contaminant level for MTBE.

The Village of Liberty notified NYS DOH of the MTBE contamination on January 8, 1993 and the public was notified on January 22, 1993 via radio, newspaper, and letter. On January 26, 1993 the well was taken out of service and the distribution system was flushed to remove MTBE contamination on January 27, 1993. From this date until June 30, 1993, Revonah Lake, an unfiltered surface water source, was used to supply drinking water to the Village of Liberty. While MTBE was not detected in any water samples collected after switching to Revonah Lake water, new Federal and State mandates enacted on June 30, 1993 required filtration of all surface waters. The new regulation was implemented to reduce microbiological contaminants and naturally-occurring organic matter often found in surface waters. NYS DEC supplied a water tanker and installed an external tap connecting to the Town of Liberty water system as alternatives for residents not wanting to drink water from Revonah Lake since it violated the new filtration requirements.

Due to new regulations and a dwindling water supply, the Village of Liberty discontinued use of Revonah Lake as a water supply on August 4, 1993. The Village resumed pumping the Elm Street well at half capacity, but demand grew throughout the autumn of 1993. An increase in demand may have pulled in water from contaminated ground supplies, resulting in a monthly average MTBE concentration exceeding the 50 $\mu\text{g}/\text{L}$ limit standard in November, 1993. To reduce the demand on the Elm Street well, a pumping station was constructed that mixed the well water with Town of Liberty water. The Village of Liberty distribution system was supplied with the blended water from November 29, 1993 through July 30, 1997, during which time MTBE levels in the distribution system remained below the 50 $\mu\text{g}/\text{L}$ drinking water standard. The well water (prior to blending) was continuously monitored for MTBE contamination and the levels of MTBE decreased to below the previous NYS DOH drinking water standard. Although MTBE levels were elevated in the summers of 1994 and 1995, the monthly average

levels only exceeded the NYS DOH standard (50 µg/L) in June and July of 1994. A single sample from June 17, 1994 showed high levels of MTBE. However, in late June 1994, the MTBE levels (81 µg/L and 79 µg/L on June 23, 1994 and June 29, 1994, respectively) in well water again exceeded the NYS DOH drinking water standard.

As of July 30, 1997, water was no longer purchased from the Town of Liberty because MTBE levels in the well fell and remained well below the NYS DOH standard (50 µg/L). The Elm Street well was operated as the Village of Liberty's sole water source until September 3, 1998. The MTBE levels remained low, even during heavy pumping, indicating that the clean-up (remedial) activities at the contaminating source were effective. A treatment plant at Lily Pond was constructed and Lily Pond became the Village's primary water supply in September of 1998. The Elm Street well has since only been used to meet seasonal periods of high demand and to maintain pressure in the distribution system.

MTBE has not been detected in the well since December of 1998. However, other chemicals including benzene, naphthalene and xylene were detected infrequently below their respective public drinking water standards between December 1998 and October 2000. Trihalomethanes (THMs), a class of chlorine disinfection byproducts, have also occasionally been detected at low levels (levels below the public drinking water standards) in water from the Elm Street well. Tetrachloroethene was also detected in well water at levels below the drinking water standard between May and October 2000, but the source of this contamination is unknown. Water testing data from 2004-2011 show no elevations in MTBE, THMs, benzene, naphthalene or xylene.

Although Lily Pond was the primary source of water from the 1920's until the Elm Street well was installed in 1960, it has some limitations. Lily Pond is shallow and has a high level of natural organic matter. Organic matter can react with chlorine during disinfection to form chemicals known as disinfection byproducts (DBPs) which include two chemical classes, trihalomethanes (THMs) and haloacetic acids (HAAs), which are regulated by the US Environmental Protection Agency (EPA) and NYS DOH. The regulation requires the annual average of quarterly THM and HAA levels to be below 100 µg/L and 80 µg/L, respectively. Although annual averages for THMs and HAAs in the distribution system had not exceeded these standards, in 2000 the NYS DOH recommended some changes in plant operation to reduce DBP formation and ensure the treatment plant would comply with new drinking water standards. In May, 2003, the Village received short-term financing in the amount of \$5.6 million dollars from the NYS Safe Drinking Water Act, State Revolving Fund, to upgrade the Village's water supply system.

2.2 MTBE Exposures and Potential Health Risks

MTBE is a volatile organic compound (VOC) that has a distinctive odor that most people find disagreeable (ATSDR, 1997). Commercial use of MTBE as a gasoline additive began in NYS in 1979 when the US EPA approved MTBE as a blending agent for octane enhancement in unleaded and premium gasoline (US EPA, 2011), and ended when NYS banned its use as of January 1, 2004 (NYS DAM, 2003).

Before it was banned in NYS, exposure to MTBE occurred from inhaling auto exhaust or gasoline fumes. While inhalation is the major route of exposure to MTBE for the general population, oral and dermal exposures can also occur when MTBE contaminates drinking water supplies. Due to its small molecular

size and solubility in water, MTBE moves more rapidly into groundwater than other constituents of gasoline (US EPA, 2011).

There are no data on the effects in people of drinking MTBE. Animal studies show that drinking MTBE causes gastrointestinal irritation, liver and kidney damage, and nervous system effects in rodents (Belpoggi, et al., 1998). There have been no studies of MTBE and cancer in humans. Studies have shown that MTBE causes liver tumors in male and female mice, and kidney and testicular tumors in male rats, via inhalation (Bird, et al., 1997). It also causes testicular tumors in male rats and lymphomas and leukemias in female rats that were given large doses directly into their stomach (Belpoggi, et al., 1998). The exposure levels in the studies cited above were much higher than the estimated exposure level in water from the Village’s Elm Street well. While some animal and human studies show reproductive and developmental effects associated with exposures to VOCs, we are not aware of any such studies specifically of MTBE exposures.

3.0 BIRTH OUTCOME REVIEW METHODS

3.1 Study Design: This investigation estimates levels of adverse birth outcomes among the population served by the Village of Liberty public water supply and compares them to levels in the general population of NYS (excluding NYC). These comparisons show whether the numbers of these outcomes are higher, lower, or about the same as what would be expected, taking account of the Village’s specific sex and age group populations over the years of the investigation. Because birth certificates contain a great deal of information about the mother and infant, the analyses of birth outcomes are also able to take account of race, education, number of previous live births, and prenatal care.

3.2 Exposure Areas and Timeframes: A map of the study’s three exposure areas is provided in Figure 1. The water district boundaries were used to define the exposure areas. To reflect multiple exposure areas and timeframes, the study analyses were conducted for five different exposure groups. Table 1 shows the estimations of differing MTBE exposure levels for each of the five exposure analysis groups. The years selected for the timeframes for the analysis groups differ from the actual exposure timeframes because birth outcomes of interest can occur not only during the exposure period, but for an additional 8-9 months after the exposure period has ended.

Water District	Outcome time period			
	1979-1985	1986-1993	1994-1999	2000-2005
LIBERTY	1. NONE-LOW	2. ELEVATED	3. LOW/VARIABLE	4. NONE
FERNDALE	1. NONE-LOW	2. ELEVATED	5. NONE	
STEVENSVILLE	1. NONE-LOW	2. ELEVATED	5. NONE	

While there is no information about MTBE levels prior to 1990, residents of all three water districts may have been exposed to potentially increasing levels of MTBE from 1979 through 1984, and to potentially higher levels of MTBE from 1985 through 1992. The year 1985 was used as the midpoint between “none to low” and “elevated” exposures because it divides the 15-year time period into nearly equal subsets. From 1993 to 1998, sampling shows that levels of MTBE were generally lower, but varying, for the Village of Liberty. Finally, no **elevated** MTBE exposures from public water were occurring for the

Village of Liberty from 1999 to 2005, and for Ferndale and Stevensville from 1993 to 2005. The time frames for the exposure groups are adjusted by one year because they represent the birth year, rather than exposure time frame. Inhalation exposures, especially while pumping gas, potentially occurred throughout the entire study period.

3.3 Identifying Health Outcomes among Exposure Area Residents: We obtained records of all births and birth defects with residential addresses within ZIP Codes 12734, 12754, 12768 and 12783. To capture records with missing ZIP Code information, we also obtained the addresses for all records in Sullivan County without a ZIP Code. Using a variety of methods (see Appendix A), we assigned each record to a location either in or out of the study area. To protect confidentiality, no maps of individual case locations can be provided. Additional information about the process of identifying and mapping individual health outcome records is provided in Appendix A.

3.4 Demographic Characteristics of the Exposure Area and Comparison Populations: Appendix Table 1 at the end of the report compares the demographic characteristics of the population of the exposure areas to the population of NYS (excluding NYC). In 2000, the populations of the Liberty, Ferndale and Stevensville water districts were 3,873, 387 and 231 persons, respectively. The populations of the Ferndale and Stevensville water districts increased by 26% and 32% respectively, between 1990 and 2000. In contrast, the population of the Village of Liberty decreased by 5% in this time period. The population of the State (excluding NYC) increased by five percent over the same time period. The age distribution and racial makeup of the study areas are mostly similar to that of NYS. All three water districts had higher Hispanic populations than the rest of NYS for both the 1990 and 2000 Census. In 2000, the percent Hispanic population in the Stevensville water district was three times more than New York State. The water districts' median incomes were considerably lower than the median income of NYS (excluding NYC) in both 1990 and 2000. The median income for the Village of Liberty was \$19,317 compared to \$35,711 for NY (excluding NYC) in 1990, and \$33,786 in Liberty vs \$47,517 in upstate NY in 2000.

3.5 Birth Outcomes: Table 2 shows the types of outcomes included in the birth outcomes review, the data sources, years of data available when data for the investigation were acquired and the timeframes used in the review.

Table 2. Outcomes, Data Sources and Years			
Type of Outcome	Data Source	Years Available	Timeframes Reviewed
Low Birth Weight, Prematurity & Growth Restriction; Sex Ratio	NYS Vital Records (Birth Certificates)	1978-2005	1979-2005
Birth Defects	NYS Congenital Malformations Registry	1983-2004	1983-2004

Figure 1. Village of Liberty, Ferndale, and Stevensville Water District Exposure Areas

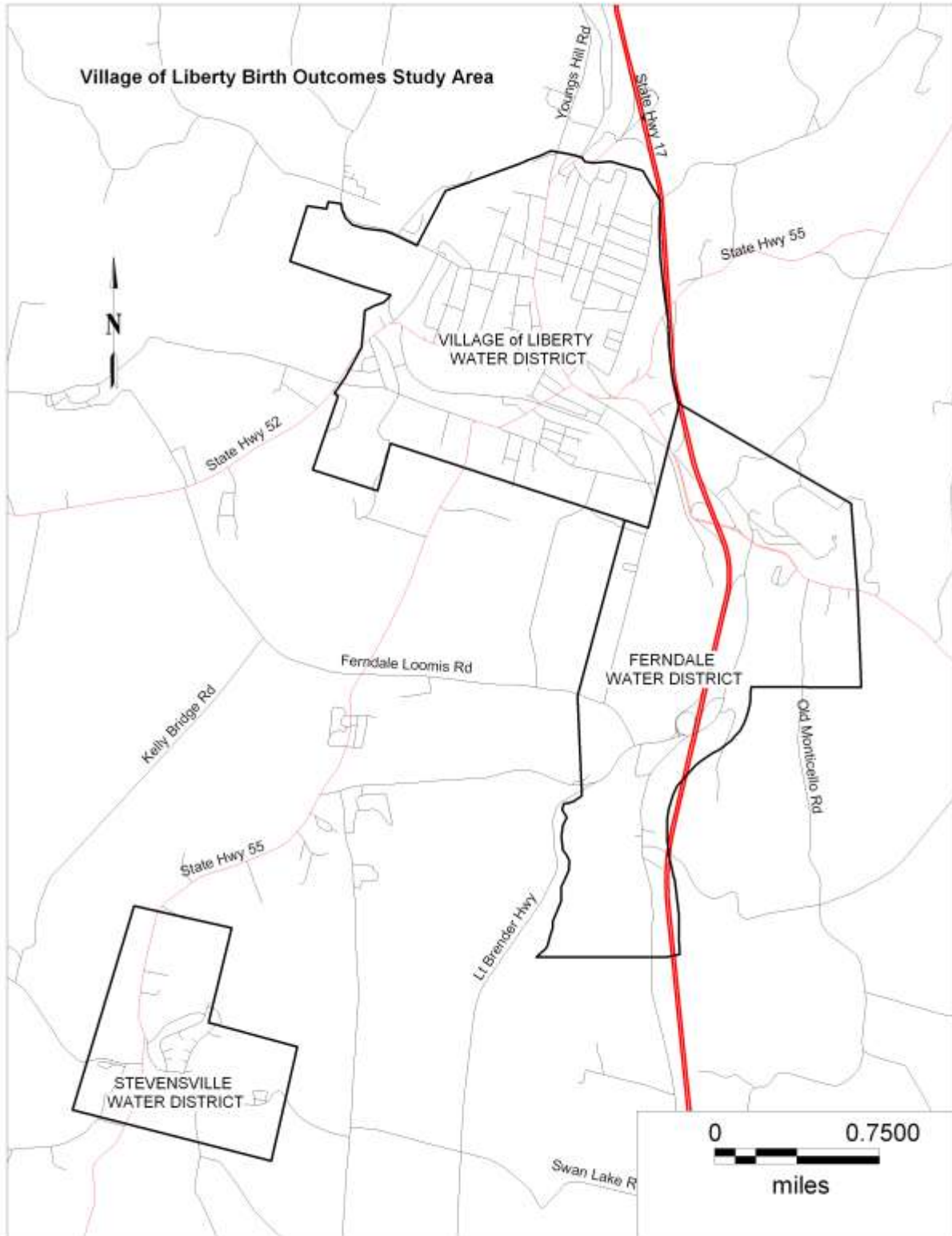


Table 3 lists the specific health outcomes and subsets evaluated for the low birth weight, prematurity, growth restriction and sex ratio outcomes as well as their basic definitions.

Table 3. Birth Weight, Prematurity, Growth Restriction, & Sex Ratio Definitions		
Birth Weight	Birth Weight Subsets	
<u>Low birth weight</u> = <2500 grams (5.5 lbs)	<u>Moderately low birth weight</u> = ≥1500 grams and <2500grams	<u>Very low birth weight</u> = <1500 grams
Prematurity	Prematurity Subsets	
<u>Pre-term</u> = < 37 weeks	<u>Moderately pre-term</u> = ≥32 and <37 weeks	<u>Very pre-term</u> = <32 weeks
Growth Restriction		
<u>Small for gestational age</u> (SGA) = birth weight below the 10 th percentile of the NYS (excluding NYC) birth weight distribution		
<u>Term low birth weight</u> (TLBW) = ≥37 weeks gestation and birth weight <2500g		
Sex Ratio = the number of male births divided by number of female births		

Table 4 lists the birth defect categories included in this review. All reportable defects were evaluated as well as specific subsets of birth defects considered to be appropriate to evaluate for VOC-exposed populations, based on current research findings. (See **Appendix Table 2** for additional information about the list of defects.) Some of the specific diagnoses included in the “total reportable defects” category have changed slightly over time, but this grouping is primarily made up of the structural birth defects.

Table 4. Birth Defect Categories
Total Reportable Defects
Structural Defects
A. Surveillance Defects
B. Neural Tube Defects
C. Total Cardiac Defects
Major Cardiac Defects
D. Cleft lip/cleft palate
E. Choanal atresia
F. Down’s Syndrome

Birth outcome information from birth records for all of NYS (excluding NYC), about 3.4 million births over the entire study period, was used to calculate the **expected** number of births with each type of birth weight, pre-term or growth restriction outcome in the exposure areas from 1979 through 2005. Only singleton births (one baby) were included in the birth weight, pre-term and growth restriction analyses because multiple births (e.g., twins, triplets) have higher risk for these adverse birth outcomes. Birth records for all births in the study area were matched to birth defect records to identify specific infants born with birth defects in the study area from 1984 to 2004. The expected number of total birth outcomes of each type for NYS (excluding NYC) was calculated and compared to the total number of birth outcomes observed. The general pattern of types of birth defects was also reviewed to look for unusual patterns in the number and types of defects. The actual number of health outcomes in the study area is called the **observed** number. Observed and expected numbers for each birth outcome are presented in the Results section.

3.6 Statistical Methods: Several of these birth outcomes, including low birth weight and pre-term birth, have been linked to having lower income and education, often called socioeconomic status. The demographics for the study area show it is different from the comparison area (NYS, excluding NYC)

which has higher socioeconomic status and lower percentages of non-white and Hispanic residents. Therefore, analyses were conducted that used information about the mother and the pregnancy to take these differences into account. **Table 5** lists the additional information from birth certificates included in the statistical models.

Sex of the infant	male	female	
Mother's age	less than 19	19-34	35+
Mothers' education	less than high school	high school-some college	4+ years college
Race category	white	non-white	
Number of previous live births	0	1	2+
Prenatal care	inadequate	intermediate	adequate

The modified Kessner Index, which combines the month the mother first got prenatal care and the number of prenatal visits she had, was used to classify her prenatal care into one of three categories: adequate, intermediate, and inadequate (Kessner, et al., 1973). The models use Poisson regression to compare the rate for each type of birth outcome in the Liberty exposure groups to rates in the general NYS population (excluding NYC), while taking these factors into account. (A very small percentage of births in the exposure groups and the comparison groups are excluded from the regression analyses because they are missing information on race, education, or other variables.) For each outcome, we present the adjusted rate ratio (RR) and its 95 percent confidence interval (CI) for exposure status.

A **rate ratio (RR)** is a measure of the association between an exposure or risk factor and a health outcome. A rate ratio greater than 1.00 suggests the exposure group is more likely to have the outcome than the comparison group. A rate ratio less than 1.00 suggests the exposure group is less likely to have the outcome than the comparison group.

The **95% Confidence Interval (CI)** is a range of rate ratios that helps us decide whether the difference between the exposed group rate and comparison group rate is likely due to chance. If the CI excludes 1.00, the RR is considered to be statistically significant. If the CI includes 1.00, the RR is not statistically significant.

4.0 BIRTH OUTCOME RESULTS

4.1 Low Birth Weight (LBW), Prematurity, Growth Restriction, Sex Ratio

A total of 1,724 births were geocoded within the study area. Of these, a total of 1,688 births among residents in the study area during 1979-2005 were used for the study. Seven percent of the study area births and eight percent of NYS (excluding NYC) births were excluded from the analysis for one of the following reasons: plural birth; missing the value for sex, gestational age, or birth weight; implausible gestational age or birth weight. Results from the Poisson regression analyses were conducted for the five exposure groups separately as well as for the exposure areas combined into two categories representing variable MTBE and post-MTBE exposure. Results are presented in **Table 6** for the two

category analyses that combined the three variable MTBE exposure groups and the two post-MTBE exposure groups. (See Table 1, page 4.)

Type of Outcome	Exposure Groups 1, 2 and 3* (Variable MTBE)					Exposure Groups 4 and 5** (Post-MTBE)				
	1979-1999					1994-2005				
	# of cases		Adjusted RR	95% C.I.		# of cases		Adjusted RR	95% CI	
	Observed	Expected		Lower	Upper	Observed	Expected		Lower	Upper
Low birth weight (LBW)	72	68.9	0.99	0.79	1.25	22	20.4	1.06	0.69	1.62
Moderately LBW	59	56.4	0.98	0.76	1.27	20	16.6	1.22	0.79	1.9
Very LBW	13	12.5	1.05	0.61	1.80	2	3.9	0.28	0.04	2.02
Preterm birth	117	105.7	1.00	0.84	1.20	29	32.1	0.89	0.62	1.28
Moderately preterm	96	85.9	1.02	0.83	1.24	25	26.9	0.92	0.62	1.36
Very preterm	21	19.7	0.95	0.62	1.45	4	5.2	0.73	0.27	1.94
Term low birth weight	30	26.8	0.98	0.69	1.40	12	7.1	1.52	0.86	2.68
Small for gestational age	131	113.7	1.05	0.89	1.25	43	32.1	1.21	0.89	1.64
Number of male births	661	660.8	--	--	--	173	187.5	--	--	--
Males/total births***	0.51	0.51	1.00	0.93	1.08	0.47	0.51	0.92	0.79	1.07

* Exposure groups 1, 2 and 3 contain Liberty, Ferndale and Stevensville water districts from 1979-1993 and just the Liberty water district from 1994-1999.

** Exposure groups 4 and 5 contain the Liberty water district from 2000-2005 and the Ferndale and Stevensville water districts from 1994-2005.

*** Ratio of males to total births. SIR is presented.

Exposure groups 1, 2 and 3 combined – Varying MTBE exposure, 1979-1999

Analyses for groups 1, 2 and 3 combined are presented here. Exposure groups 1, 2 and 3 all had unknown, low, elevated, or variable MTBE levels at some point. In this combined group, all birth outcomes showed rate ratios that were very close to 1.00, i.e., no difference between the rate and the upstate comparison rate. None of these RRs were statistically significant, and the highest RR is 1.05 (CI: 0.89 - 1.25).

Exposure groups 4 and 5 combined – Post-MTBE exposure, 1994-2005

Exposure groups 4 and 5 are combined for analysis and represent a post-MTBE exposure group. There were no statistically significantly elevated birth outcomes for this combined exposure group. The RRs for low birth weight, and its subcategory, moderately low birth weight were both elevated, but not statistically significant. The two growth restriction outcomes, term low birth weight and small for gestational age were also elevated, but not statistically significant. Term low birth weight had the highest RR (1.52, CI: 0.86 - 2.68), based on 12 cases observed in the exposure area versus 7 expected.

Results are presented in **Table 7a and 7b** separately for the three exposure groups with potential MTBE exposure.

Table 7a. Low Birth Weight, Prematurity and Growth Restriction Results: Exposure groups 1 & 2

Type of Outcome	Exposure Group 1* (None to Low MTBE)					Exposure Group 2** (Elevated MTBE)				
	1979-1985					1986-1993				
	# cases		Adjusted RR	95% C.I.		# cases		Adjusted RR	95% CI	
	Observed	Expected		Lower	Upper	Observed	Expected		Lower	Upper
Low birth weight (LBW)	18	21.9	0.73	0.46	1.16	35	28.7	1.14	0.82	1.6
Moderately LBW	16	18.1	0.78	0.48	1.28	27	23.4	1.05	0.72	1.55
Very LBW	2	3.8	0.49	0.12	1.95	8	5.3	1.57	0.79	3.14
Preterm birth	27	32.2	0.71	0.49	1.04	62	45.6	1.24	0.97	1.59
Moderately preterm	24	26.1	0.79	0.53	1.18	47	36.9	1.17	0.88	1.56
Very preterm	3	6.1	0.4	0.13	1.24	15	8.7	1.54	0.93	2.55
Term low birth weight	11	9	1.05	0.58	1.89	11	11.1	0.88	0.49	1.58
Small for gestational age	46	35.7	1.17	0.87	1.56	50	47.7	0.96	0.73	1.27
Number of male births	216	210	--	--	--	293	281.3	--	--	--
Males/total births***	0.53	0.51	1.03	0.9	1.18	0.53	0.51	1.04	0.93	1.17

* Liberty, Ferndale and Stevensville water districts. None-Low levels of MTBE.

** Liberty, Ferndale and Stevensville water districts. Elevated levels of MTBE.

***Ratio of males to total births. SIR is presented.

Exposure group 1 – Liberty, Ferndale and Stevensville water districts, 1979-1985

There were a total of 439 births in exposure area 1 before excluding multiple births and births with missing covariates. Term low birth weight and small for gestational age were slightly elevated, and neither elevation was statistically significant (RR 1.05, CI: 0.58 - 1.89 and RR 1.17, CI: 0.87 - 1.56). Slightly more males were born than were expected, but the difference was not statistically significant.

Exposure group 2 – Liberty, Ferndale and Stevensville water districts, 1986-1993

A total of 565 births occurred in exposure group 2. In this exposure group, all of the birth outcomes *except* term low birth weight and small for gestational age are elevated, but none are statistically significant. Preterm birth is the outcome with an elevation closest to being significant (RR 1.24, CI: 0.97 - 1.59). A review of the year of birth for each preterm birth during this eight-year period showed that approximately one-half of the preterm births occurred during just two years, 1991 and 1992. To evaluate this pattern further, the analysis was repeated using the clinical gestational age of the baby, which is the estimate of gestational age provided by the clinician, also available on birth certificates. Evaluation of the preterm births using this alternative estimate of gestational age showed no evidence of an elevation (data not shown). (Gestational age is computed using date of last menstrual period and date of birth. Clinical gestational age is a single data element provided as an alternative estimate of gestational age using clinical examination information.)

Table 7b. Low Birth Weight, Prematurity and Growth Restriction Results: Exposure Group 3					
Type of Outcome	Exposure Group 3* (Lower/Variable MTBE)				
	1994-1999				
	# cases		Adjusted RR	95% C.I.	
	Ob- served	Ex- pected		Lower	Upper
Low birth weight (LBW)	23	18.3	1.07	0.69	1.66
Moderately LBW	18	14.8	1.11	0.69	1.79
Very LBW	5	3.4	0.89	0.29	2.76
Preterm birth	30	27.9	0.95	0.65	1.37
Moderately preterm	26	23.0	1.03	0.70	1.53
Very preterm	4	4.9	0.57	0.19	1.78
Term low birth weight	8	6.7	1.05	0.53	2.10
Small for gestational age	35	30.4	1.06	0.76	1.47
Number of male births	152	169.6			
Males/total births**	0.46	0.51	0.90	0.76	1.05
* Liberty water district. Lower/Variable levels of MTBE.					
** Ratio of males to total births. SIR is presented.					

Exposure area 3 – Liberty water district, 1994-1999

A total of 333 births were identified in exposure group 3. Exposure group 3 shows a mixture of elevations and deficits for the outcomes and no results are statistically significant. The rate ratios for very low birth weight births, preterm births, and very preterm births are all below 1.

Table 8 shows results for exposure groups 4 and 5, the post-MTBE exposure areas and timeframes.

Table 8. Low Birth Weight, Prematurity and Growth Restriction Results: Exposure Groups 4 & 5 (post-MTBE)										
Type of Outcome	Exposure Group 4* (post-MTBE)					Exposure Group 5** (post-MTBE)				
	2000-2005					1994-2005				
	# cases		Adjusted RR	95% C.I.		# cases		Adjusted RR	95% CI	
	Ob-served	Ex-pected		Lower	Upper	Ob-served	Ex-pected		Lower	Upper
Low birth weight (LBW)	21	17.7	1.16	0.75	1.79	1	2.8	0.41	0.06	2.91
Moderately LBW	20	14.3	1.40	0.91	2.18	0	2.2	-	-	-
Very LBW	1	3.3	-	-	-	1	0.5	2.47	0.35	17.51
Preterm birth	24	27.8	0.83	0.56	1.24	5	4.5	1.20	0.50	2.88
Moderately preterm	22	23.3	0.91	0.60	1.39	3	3.7	0.85	0.28	2.65
Very preterm	2	4.5	0.42	0.10	1.68	2	0.7	3.04	0.76	12.14
Term low birth weight	12	6.2	1.77	1.00	3.11	0	1.0	-	-	-
Small for gestational age	37	27.6	1.21	0.87	1.68	6	4.5	1.32	0.59	2.93
Number of male births	143	161.4				30	26.1			
Males/total births	0.45	0.51	0.89	0.75	1.04	0.59	0.51	1.15	0.77	1.64
* Liberty water district. No MTBE detected.										
** Ferndale and Stevensville water districts. No MTBE detected.										
*** Ratio of males to total births. SIR is presented.										

Exposure group 4 – Liberty water district, 2000-2005

A total of 322 births occurred in exposure group 4. Low birth weight, moderately low birth weight, and small for gestational age are all elevated but not statistically significantly. The RR for term low birth weight (RR 1.77, CI: 1.00 - 3.11) is statistically significantly elevated, at the borderline of statistical significance. No RR was calculated for very low birth weight because there were no outcomes included in the analysis for exposure group 4.

Exposure group 5 – Ferndale and Stevensville water districts, 1994-2005

Exposure group 5 is the smallest exposure group, with 51 total births. The RRs for exposure group 5 showed a mix of elevations and deficits but none were statistically significant. No RRs were calculated for moderately low birth weight and term low birth weight because there were no outcomes included in the analysis.

4.2 Birth defects

Seventy birth defects were detected in the five exposure groups over 22 years (1983-2004). A variety of defects were represented in the total, with musculoskeletal defects, heart defects and defects of the genitourinary system reported most frequently. This pattern reflects the usual pattern of birth defects. (Musculoskeletal and genitourinary system defects are not reported separately in the tables because these types of defects have not been associated specifically with exposures to volatile organic compounds.) After excluding births with incomplete information, there were a total of 66 defects and 65.6 were expected. Fifty-nine of the 66 total defects were observed in the exposure groups with potential MTBE exposures. Additional analyses were conducted for these three groups combined and are presented below in **Table 9**. The number of births in the two post-MTBE exposure groups are very small for this type of analysis but are presented in **Table 10** for comparison with the MTBE exposure group analysis.

Type of Outcome	Exposure Groups 1, 2 and 3* (1983-1999)				
	# cases		Adjusted RR	95% C.I.	
	Observed**	Expected		Lower	Upper
All birth defects	59	56.1	1.06	0.82	1.37
Structural defects	53	47.0	1.15	0.89	1.52
Surveillance defects	28	25.1	1.16	0.80	1.68
All cardiac defects	8	9.8	0.84	0.42	1.68
Major cardiac	2	2.2	0.91	0.23	3.63
Conotruncal	2	0.9	2.41	0.60	9.64
Cleft lip/cleft palate	2	1.2	1.74	0.44	6.98
Choanal atresia	0	0.2	-	-	-
Neural Tube defects	1	0.5	1.91	0.27	13.56
Downs Syndrome	1	0.4	2.49	0.35	17.72
* Exposure groups 1, 2 and 3 contain Liberty, Ferndale and Stevensville water districts from 1983-1993 and Liberty water district from 1994-1999.					
** Number of observations used in analysis					

Type of Outcome	Exposure Groups 4 & 5* (1994-2005)				
	# cases		Adjusted RR	95% C.I.	
	Observed**	Expected		Lower	Upper
All birth defects	7	9.5	0.77	0.37	1.62
Structural defects	7	8.3	0.90	0.43	1.89
Surveillance defects	4	5.5	0.78	0.29	2.08
All cardiac defects	1	2.4	0.45	0.06	3.17
* Exposure groups 4 and 5 contain the Liberty water districts from 2000-2005 and the Ferndale and Stevensville water districts from 1994-2005.					
** Number of observations used in analysis					

There were no statistically significant elevations or deficits of any birth defect category in Exposure Groups 1, 2, and 3 combined. There were nine cardiac birth defects in exposure groups 1, 2 and 3. One record dropped out of the analysis because it was missing a covariate, leaving a total of eight cardiac birth defects in the Poisson regression analysis. Records that are missing information from the birth certificate needed for the analysis are left out of both the exposure and comparison area births. Only two of the eight cardiac defects were major cardiac defects and these were both conotruncal defects. These two defects occurred among births in Exposure group 3, after 1995, which is not the exposure group considered to have the highest MTBE exposures. In exposure groups 4 and 5, the post-MTBE exposure groups, there are also no statistically significant elevations or deficits for any category of birth defects. For all exposure groups combined there were also no statistically significant elevations in birth defects.

4.3 Birth Outcome Results Summary

This health outcomes review found no statistically significant elevations or deficits of adverse birth outcomes (LBW, prematurity, growth restriction, and sex ratio) in the analyses that combined the three MTBE exposure groups and compared them to statewide (excluding NYC) births during 1979-2005. In the analyses of these three specific exposure groups based on gradations of potential MTBE exposure levels, none of the MTBE exposure groups showed any statistically significant excesses or deficits. In the exposure group with the highest potential MTBE exposures, exposure group 2, there are a greater number of elevated RRs, and higher RRs, than for exposure groups 1 and 3 that experienced less potential MTBE exposure. The RR for preterm births of 1.24 (CI: 0.97-1.59) in exposure group 2 is close to being statistically significant and is based on 62 preterm births observed compared to 46 expected.

In the analyses of exposure groups 4 and 5, with no MTBE exposures from the Elm Street well, there is one statistically significant elevation. This elevation is for term low birth weight births (RR 1.77, CI: 1.00 - 3.11) in exposure group 4, and is at the borderline of statistical significance. Exposure group 4 includes births in the Liberty water district between the years 2000 and 2005. Exposure group 4 births are not expected to have been exposed to levels of MTBE above the drinking water standard at the time. This exposure group was provided water from Lily Pond. Of the many statistical tests conducted for this review, only this one showed a statistically significant result. Although statistically significant, this result may have been due to chance.

There were no statistically significant excesses (or deficits) of birth defects during the period when MTBE exposures are expected to have occurred, or in the later, post-MTBE time period. There was no unusual pattern of types of birth defects observed and no suggestive pattern of elevations for the subsets of defects associated with volatile organic compounds (VOCs) in other studies.

5.0 CANCER REVIEW METHODS

5.1 Study Plan

The cancer investigation was designed to determine whether the number of cancer cases among people residing in the study area was unusual. To do this, the number of cases actually diagnosed among residents of the study area was compared with the number of cases one would expect to find, if cancer rates in the study area were the same as in similar areas of the state.

5.2 Study Area and Time Period

The study area consisted of ZIP Codes 12754 (Liberty) and 12768 (Parksville), Sullivan County (see **Figure 2**). Following confidentiality protocols in place when this investigation was begun, the sparsely populated ZIP Code 12768 was combined with neighboring ZIP Code 12754 and included as part of the study area because these two ZIP Codes had been combined in previously released data. The time period for the investigation of cancer incidence was 1990 through 2003, the most recent period for which cancer reporting was considered complete for analysis within small geographic areas at the time work on the study was initiated.

5.3 Identification of Observed Incident Cancers

To proceed with the investigation, we identified all cases of cancer diagnosed among people residing in the study area during the time period of the study. The source for these data was the New York State Cancer Registry. The Cancer Registry contains information on all cases of cancer reported to the NYSDOH, as mandated by law. The computerized Cancer Registry files are continuously updated to reflect information gained from multiple reports on the same cancer. Cancer incidence data presented in this report represent cancer cases diagnosed from 1990 through 2003, with information on these cases updated as of March 2006.

Variation in cancer incidence among different geographic areas reflects not only true differences in cancer incidence, but also differences in how cancer is diagnosed, treated, and recorded in different areas of the state. The completeness and accuracy of the Cancer Registry depends upon reporting from hospitals. The Cancer Registry has been certified as more than 95% complete by the North American Association of Central Cancer Registries (Ellison JH, et al., 2005).

To identify all cancer cases within the study area, a listing of all cancer cases diagnosed in the ZIP Codes serving the study area was obtained from the Cancer Registry. These cases were then grouped by age, sex and type of cancer. These are referred to as "observed" cases.

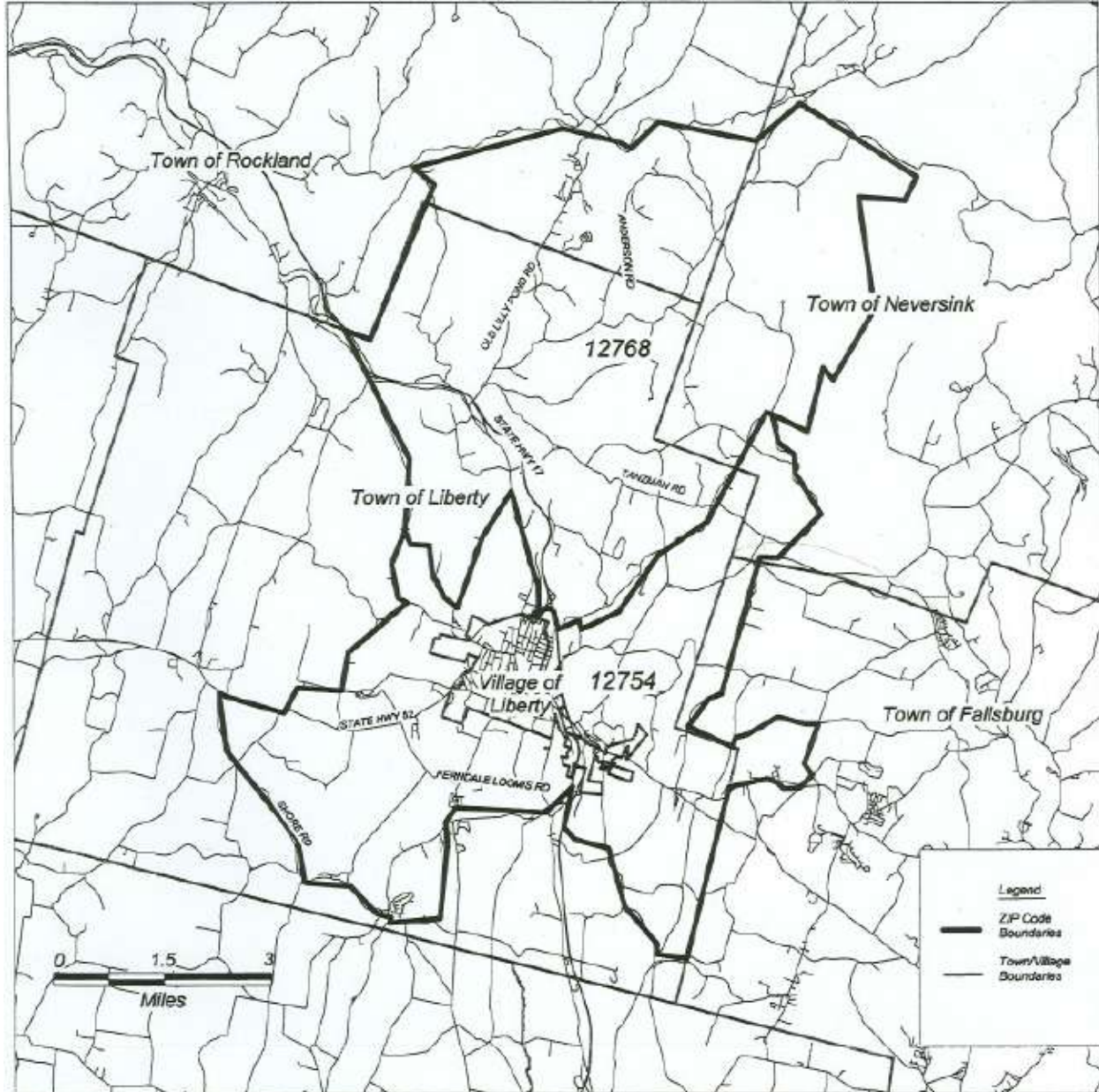
5.4 Calculation of Expected Incident Cancers

To determine whether the number of observed cases was unusual, we calculated the number of cancers that would be expected in the study area. This calculation takes into account the population size and the age and sex distribution of the study area. The expected number of cancer cases was calculated by applying cancer incidence rates by age and sex for a reference area to the estimated population of the study area by age and sex. The reference area selected for this investigation was New York State, exclusive of New York City. The population of the study area for 1990-2003 was estimated using data from Claritas, a commercial vendor that provides demographic estimates and projections based on United States Census data and geography.

5.5 Types of Cancer (Anatomic Sites) Studied

Seventeen of the most common types of cancer were examined among males, including lung, colorectal, prostate, and bladder cancers, and lymphomas and leukemias. Nineteen of the most common types were examined among females. In addition to the sites examined for males (except prostate), cancers of the breast and female reproductive organs were also examined for females.

Figure 2. Map of Cancer ZIP Code Study Area



5.6 Statistical Testing

The probability that chance alone could explain an increase or decrease in the observed number of cancer cases compared to the expected number was evaluated based on the Poisson distribution (Molina, EC, 1973). (In statistics, the Poisson distribution describes a process where a rare event occurs in a large population.) The results tables show standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) for each cancer site studied in males and females. The SIR is the ratio between the number of cases observed and the number of cases expected. An SIR greater than 1.00 indicates that

the number of cases observed is greater than the number of cases expected. An SIR less than 1.00 indicates that the number of cases observed is less than the number of cases expected. The 95% CI for the SIR is a range of SIRs that helps us visualize whether the difference between the number of cases observed and the number of cases expected is likely to be due to chance. If the 95% CI excludes 1.00, the SIR is considered to be statistically significant. If the 95% CI does not exclude 1.00, the SIR is not considered to be statistically significant. Non-significant excesses or deficits were considered to represent random variations in observed patterns of disease.

6.0 CANCER REVIEW RESULTS

A total of 713 cancers (344 males/369 females) were identified among all males and females residing in the study area between 1990 and 2003. For all anatomical sites combined, the total of 344 cases of cancer observed in males was not statistically significantly different from the 340 cases expected. Among females, the total of 369 cancer cases observed was more than the 336 cases expected but the difference was not statistically significant. These results are summarized in Table 11.

The most common types of cancer observed among males included prostate, with 91 cases observed (97 cases expected); lung, with 62 cases observed (56 cases expected); and colorectal, with 41 cases observed (42 cases expected). Fewer than six cases were observed for several types of cancer including cancers of the pancreas, testis, brain and other parts of the nervous system, thyroid, and for multiple myeloma. (To protect patient confidentiality, for cancer sites with fewer than six observed cases, the specific numbers of observed cases have not been indicated.) Among all cancer sites examined, a statistically significant excess was found in the number of males with leukemia (18 cases observed, 10 cases expected). As is usually seen with leukemia, the majority of cases were found in people over the age of 65, and the most frequently diagnosed subtypes were acute myelogenous leukemia (AML) and chronic lymphocytic leukemia (CLL). A statistically significant deficit was found in the number of males with multiple myeloma (0 cases observed, 4 cases expected). No other individual site showed a statistically significant difference.

The most common types of cancer observed among females included breast, with 79 cases observed (92 cases expected); lung, with 65 cases observed (46 cases expected); and colorectal, with 51 cases observed (46 cases expected). Fewer than six cases were observed for several other types of cancer, including cancers of the esophagus, liver and intrahepatic bile duct, larynx, kidney and renal pelvis, brain and other parts of the nervous system, and for multiple myeloma. Among all cancer sites examined, a statistically significant excess was found in the number of females with lung cancer. No other individual site of cancer among females showed a statistically significant difference.

Types of cancer associated with MTBE exposure in animals include cancers of the kidney, liver, and testis, leukemias and lymphomas (ATSDR, 1996; Belpoggi, et al., 1998). In the study area, numbers of cases of kidney cancer, testicular cancer, and lymphomas were close to the numbers expected in both males and females. (Specific findings for testicular cancers are not shown in Table 11 because the observed numbers are fewer than six, the cut-off used for protecting confidentiality.) The number of cases of liver and intrahepatic bile duct cancer was high in males but it was not statistically significant. The number of females with this cancer was small but it was close to the number expected. Additional information on the leukemia findings is presented below, and information on the other types of cancer associated with MTBE exposure in animals is presented in Appendix B.

Table 11: Observed and Expected Numbers of Incident Cancer Cases

BUREAU OF CANCER EPIDEMIOLOGY
 NEW YORK STATE DEPARTMENT OF HEALTH
 Observed and Expected Numbers of Incident Cancer Cases,
 ZIP Codes 12754 and 12768
 Sullivan County, New York, 1990-2003
 New York State exclusive of New York City Standard 1990-2003

SITES (ICD-O-2) ^a	MALES					FEMALES				
	# cases		SIR	95% C.I.		# cases		SIR	95% CI	
	Ob- served	Ex- pected		Lower	Upper	Ob- served	Ex- pected		Lower	Upper
All Sites ^d	344	340	1.01	0.91	1.12	369	336	1.10	0.99	1.22
Oral Cavity / Pharynx	9	9	1.06	0.48	2.00	6	5	1.23	0.45	2.67
Esophagus	7	5	1.40	0.56	2.88	– ^e	2	– ^e	– ^e	– ^e
Stomach	8	8	1.04	0.45	2.04	7	5	1.32	0.53	2.73
Colorectal	41	42	0.98	0.70	1.33	51	46	1.10	0.82	1.45
Liver / Intrahepatic Bile Duct	8	4	2.02	0.87	3.98	– ^e	2	– ^e	– ^e	– ^e
Pancreas	– ^e	9	– ^e	– ^e	– ^e	11	10	1.07	0.54	1.92
Larynx	8	5	1.61	0.69	3.17	– ^e	1	– ^e	– ^e	– ^e
Lung / Bronchus	62	56	1.10	0.85	1.42	65*	46	1.41	1.09	1.79
Female Breast						79	92	0.86	0.68	1.07
Cervix uteri						11	6	1.93	0.96	3.45
Corpus Uterus / Uterus (not otherwise specified)						20	20	1.01	0.62	1.56
Ovary						13	12	1.05	0.56	1.79
Prostate	91	97	0.94	0.75	1.15					
Testis	– ^e	3	– ^e	– ^e	– ^e					
Urinary Bladder (including in situ)	26	26	0.99	0.65	1.45	11	11	1.03	0.51	1.84
Kidney / Renal Pelvis	7	10	0.69	0.28	1.43	– ^e	7	– ^e	– ^e	– ^e
Brain / Other Nervous System	– ^e	5	– ^e	– ^e	– ^e	– ^e	5	– ^e	– ^e	– ^e
Thyroid	– ^e	2	– ^e	– ^e	– ^e	7	6	1.15	0.46	2.38
Lymphomas	16	15	1.04	0.59	1.68	17	15	1.14	0.66	1.82
Multiple Myeloma	0*	4	0.00	0.00	0.70	– ^e	4	– ^e	– ^e	– ^e
Leukemias	18*	10	1.75	1.04	2.77	7	9	0.81	0.32	1.67

^aClassification of site is based on ICD for Oncology, 2nd Edition (Percy et al., 1990).

^bData were obtained from the New York State Cancer Registry (database as of March 2006).

^cExpected numbers are based on standard cancer incidence rates by age and sex for NYS, exclusive of NYC. Standard rates are applied to the total 1990-2003 study population (55,386 males and 58,554 females) to obtain expected numbers of cases.

^dIncludes observed and expected numbers of cases at sites of cancer not listed below.

^eThe number is not shown to protect patient confidentiality.

*The number of cases observed is significantly different from the number expected based on statistical testing against the Poisson distribution at a significance level (two-tailed) of 0.05.

6.1 Statistically Significant Findings

This study found that the total number of cancer cases diagnosed among males residing in the study area was close to the number of cases expected. The total number of females diagnosed with cancer was higher than expected but it was not statistically significant. When individual types of cancer were examined separately, a statistically significant excess was found in the number of males diagnosed with leukemia and in the number of females diagnosed with lung cancer.

Leukemia: In this current investigation of cancer in the Liberty area, the number of males diagnosed with leukemia was statistically significantly higher than expected. The number of females diagnosed with leukemia was slightly lower than the number expected. Leukemia is one type of cancer associated with MTBE exposure in animals (Belpoggi, et al., 1998). The animal studies showed associations between MTBE exposure and lymphocytic leukemias, in female rats only. It is not known if these findings regarding leukemia in rats have any relevance for human cancers (McGregor, 2006).

Leukemia can occur at any age but is ten times more common in adults than in children. More than half of all leukemia cases occur in people over the age of 65 (Ellison, et al., 2005). The ages of the males in the current study who were diagnosed with leukemia ranged from early childhood to the elderly. Two-thirds of the cases were diagnosed after age 65. When 10-year age groups (0-14 years, 15-24 years, 25-34 years, etc.) were examined separately, no particular age group had a statistically significant excess. The number of cases diagnosed was stable with no more than three cases diagnosed in any given year.

A variety of types of leukemia were diagnosed in this Liberty- area study, the most frequent being acute myeloid leukemia (AML) followed by chronic lymphocytic leukemia (CLL). Other types of leukemia observed in this investigation included acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML), and leukemias of unspecified type. AML and CLL are the most common types of leukemia diagnosed among adults (Howlader, et al., 2008). All of the small number of children who were diagnosed with leukemia in the current study were diagnosed with acute lymphoblastic leukemia (ALL). This is the most frequently diagnosed type of leukemia among children.

Due to the statistically significant excess number of men diagnosed with leukemia, medical records from the admission at which leukemia was diagnosed were requested directly from the hospitals for all the males and females diagnosed with leukemia. Medical records were reviewed to confirm the diagnosis and to obtain additional information such as the medical history, family history and occupation. Records were received for 14 of the 18 males (78%) and for 6 of the 7 females (86%). Records were not received for some of the cases because the records could not be found, had been destroyed, the patient was reported by an out-of-state hospital, or the case was identified from the death certificate only, with no reporting hospital. All of the individuals whose medical records were received were confirmed to have some form of leukemia. Three of the men for whom medical records were unavailable had a clinical diagnosis only or it was not known whether the diagnosis was confirmed by biopsy, leaving the possibility that any or all of these cases may not have been leukemia. If one or more of these individuals did not have leukemia then the number of cases diagnosed in the study area would not be statistically significant.

Leukemia is associated with some occupational exposures, in particular, long term workplace exposure to benzene, and exposure to high doses of ionizing radiation. To assess possible occupational exposure,

the current or usual occupation of the individuals diagnosed with leukemia in the study area was determined from Cancer Registry files, death certificates and medical records. These data are limited to only a single occupation for each cancer patient and may not reflect the complete occupational history. Occupational data was available for about 70% of the adults. A variety of occupations were found including blue collar and white collar. No two individuals had the same employer. Specific occupations with possible exposures to substances or processes that have been associated with leukemia were found. The numbers of these were small, however, and could not account for the excess in cases.

Other risk factors for leukemia include Down syndrome, other genetic abnormalities, certain anti-cancer drugs, smoking and possibly a high weight at birth. A review of the medical records showed that a small number of the individuals with leukemia had one or more of these risk factors.

The residence at diagnosis of each of the males and females diagnosed with leukemia was marked on a street map of the study area. This was done to determine whether there was any geographic clustering of cases. One of the individuals could not be plotted due to insufficient street address information. A majority of them (about 75%) resided in the Village, with no obvious concentration in any particular area in the Village. According to the United States Census, in 2000 approximately 50% of the population of the study area lived within the village with the remaining 50% living in one of the two ZIP Codes in the study area but outside of the Village. It appears that all of the individuals who were located within the Village lived in areas that received their water from the Elm Street well.

Cancer of the Lung and Bronchus: In this study, the number of cases of cancer of the lung and bronchus diagnosed among females was statistically significantly higher than expected. The number of males diagnosed with this cancer was close to expected. This type of cancer is not known to be associated with MTBE exposure in animals.

The ages of these females ranged, in years, from the late 30s to the elderly with an average age of 70. About two-thirds of the cases were diagnosed after age 65. When individual 10-year age groups were examined separately, a statistically significant excess was found in females age 65-74 years. For all other age groups the observed number of cases was close to expected. The numbers of individuals diagnosed was stable from 1990 through 1997 and then increased the next two years. From 2000 to 2003, the numbers decreased to what was seen prior to the rise.

Cancer of the lung and bronchus is one of the most common cancers among New Yorkers with smoking being the most common cause. A majority of the women who were diagnosed with lung cancer and had a known smoking status were current or previous smokers. Some research studies show that exposure to other peoples' cigarette smoke (second-hand smoke), exposure to radon gas, and exposure to asbestos also increase the risk for this cancer. Other studies suggest a link between lung and bronchus cancer and working with certain chemicals, such as arsenic and chromium. Studies also show a possibility that exposure to silica, substances in foundries, processing coal, and some other chemicals may increase the risk of this cancer especially in smokers. An association has also been shown between having a medical history of some lung diseases and getting lung cancer.

The residence at the time of diagnosis of each of the females diagnosed with lung cancer was marked on a street map of the study area to look for any geographic clustering of cases. Five of the residences could not be plotted due to insufficient street address information. Residences were found to be scattered throughout the study area with approximately 50% of the females residing in the Village.

Plotting the residential addresses on a map did not show any evidence of unusual geographic distribution, although some individuals were residents of nursing homes and senior citizen housing.

6.2 Geographic Locations of MTBE-Associated Cancer Types and Cancer Types Showing Elevations

The address at the time of diagnosis was plotted on a map of the study area for males and females diagnosed with the types of cancer associated with MTBE exposure in animals as well as any cancers that were statistically significantly higher than expected. These maps were then compared with a map of the three water districts. Not all of the cases that were plotted were located in one of the water districts. About 80% of the men and 70% of the women diagnosed with leukemia resided in one of the water districts. For the remaining cancers the percentage of cases located in one of the districts varied but was no higher than two-thirds.

6.3 Cancer Incidence for the Earlier Time-Frame, 1980-89

Because of the cancer incidence elevations observed for 1990-2003, a review of cancer incidence for the previous ten years, 1980-1989, was conducted. The results are presented in Appendix Table 3. There were no statistically significant elevations for any type of cancer in this earlier time period. A total of 227 cases of cancer were observed among men and 233 cases were expected based on the population of the study area. For women, a total of 221 cases were observed and 222 cases were expected, based on the population of the study area. The types of cancer that were elevated in the 1990-2003 study period were not statistically significantly elevated in the earlier time period. In particular, there were fewer cases than expected for leukemia among males but this difference was not statistically significant. There were more lung cancer cases among both males and females than expected, but neither elevation was statistically significant.

7.0 BIRTH OUTCOMES REVIEW AND CANCER REVIEW: DISCUSSION AND LIMITATIONS

Population Mobility and Disease Latency: This type of review evaluates diagnoses that occurred while people were living in the study exposure area. Because the residence of the mother at the time of the birth was taken from the birth certificate, mothers who lived in the study area during their pregnancy but moved out of the study area before giving birth were not included in the review. Conversely, mothers who moved into the study area shortly before their child's birth were included in the review even though most of the pregnancy occurred outside of the study area. Similarly for cancer, people who lived for many years in the area but left before diagnosis are not included in the review.

For outcomes, such as cancer, with long latency periods between exposure to a carcinogen and a potentially related cancer diagnosis, it is difficult to assess the outcome in relation to past exposures that may have occurred many years before. The comparatively short time between potential prenatal exposures and the diagnosis of adverse birth outcomes increases the ability of a birth outcome study to assess the outcome in association with potential residential exposures.

Limited Information: Most environmental health studies face the challenge of limited information about actual exposures. For this review, information was available about the Village of Liberty and Ferndale and Stevensville water supplies in general, but the precise details of the specific timeframes and levels of exposure in households were not available. Although there was sufficient information to know that

drinking water was a potential source of exposure to MTBE for those using the Elm Street well, there was not enough information to identify which individuals in the study were exposed and to identify specific levels of MTBE in household drinking water.

A health outcomes review often cannot take into account personal information that may be related to the health outcomes, such as medical history, dietary and lifestyle choices (e.g., tobacco use), and occupational exposures, because the existing data do not include this information. Because birth certificates contain a great deal of information about the mother and infant, this review of adverse birth outcomes was able to take some individual characteristics into account, such as race, education, number of previous live births, and prenatal care. Cancer records were used to examine details for cases of the types of cancer that were elevated, but this type of information is not complete enough to be used in the overall analyses.

Statistical considerations: Statistical tests were performed (95 percent confidence intervals) for more than 20 individual birth and cancer outcomes. For each test, there is a five percent (1 in 20) chance that we will conclude that an elevation or deficit is significant when, in fact, it is not. In other words, it is expected that when conducting 20 different statistical tests, one result will turn out to be statistically significant by chance alone.

Another consideration is the statistical power of the statistical test, which is the chance that you will be able to detect a statistically significant elevation or deficit when, in fact, it exists. Statistical power increases as the population size, i.e., number of expected cases increases. For some rare health outcomes, such as specific birth defects and cancer types, it is unlikely that a small population will provide enough cases to detect elevations, even if they truly exist. As a general guideline, if the population is large enough that the expected number is 12 or more, and there is actually a doubling of risk in the exposed population, there is 80% power, or 80% probability that the study will show a statistically significant elevation.

Another limitation related to study population size is the problem of interpreting findings when the number of cases is very small. For example, when a population is very small, the expected number of cases may be a fraction of a case (such as 0.25 cases). If only one case is observed, the excess may appear extraordinarily high (in this hypothetical example, four times higher than expected); if no cases are observed, then it would appear that there was a deficit. Therefore, when the numbers of observed and expected cases are very small, the study's conclusions can change greatly based on the addition or subtraction of one or two cases and the results of statistical tests must be interpreted with caution.

8.0 CONCLUSIONS

When the three exposure groups with some potential exposure to MTBE from the Elm Street well were combined, no type of adverse birth outcome was statistically significantly elevated. However, in separate analyses of these three exposure groups with potentially differing levels of MTBE exposures, there were some results suggesting elevated risks in the exposure group with the highest potential exposures to MTBE, group 2. In this group, there were more rate ratios showing elevations, and although not statistically significant, these rate ratios were of higher magnitude than in the other MTBE exposure categories. In the highest potential exposure group, the elevation for preterm births (62 observed, 46 expected) produced a rate ratio of 1.24 that was close to being statistically significant (CI: 0.97-1.59). In order to address this pattern of elevated preterm births, we replicated the analysis using

the clinical gestational age. The pattern of elevated preterm births was not confirmed by this analysis. Also in this highest potential exposure group, the two adverse birth outcome categories showing the most elevated rate ratios were the categories with the smallest numbers and very low statistical power for detecting an elevation. These categories are “very low birth weight” (RR 1.57, CI: 0.79 - 3.14) and “very preterm” (RR 1.54, CI: 0.93 - 2.55). (These categories would include many of the same births.)

Analyses of birth outcomes among the two exposure groups with no elevated MTBE exposures from the Elm Street well produced one statistically significant elevation. This elevation of term low birth weight was just above the borderline for statistical significance and occurred among births in the Liberty Water district from 2000-2005, after MTBE exposures from the Elm Street well ended (RR 1.77, CI: 1.00 - 3.11).

A total of 66 birth defects were included in the analysis and 65.6 were expected. A variety of birth defects were represented in the total, with musculoskeletal defects, heart defects and defects of the genitourinary system reported most frequently. There were no statistically significant excesses (or deficits) of birth defects during the period when MTBE exposures are expected to have occurred or in the later, post-MTBE time period. There was nothing unusual noted about the pattern of birth defects.

Regarding the cancer findings, leukemia is the one type of cancer associated with MTBE exposures in animals that was statistically significantly elevated in this investigation for the years 1990-2003. The elevation was only among men, with 18 cases observed versus 10 cases expected. The lack of an elevation of leukemia diagnoses in the earlier time period, 1980-1989, is consistent with the interpretation that a latency period, or time-lag, produced elevated leukemia incidence only during the more recent time period. The majority of the men diagnosed with leukemia lived in the area supplied by water from the Elm Street well, as would be expected based on the population distribution. Only a small proportion of them had known individual risk factors. The pattern of age at diagnosis for the men with leukemia was not unusual. Given the number of individual types of cancer evaluated, it is possible that this statistically significant elevation occurred by chance. In addition, most cancers, including leukemia, have more than one possible cause, and this study did not have enough information available to identify and evaluate all other possible causes in this population.

This type of review cannot prove a link between cause and effect. Similarly, the findings, whether they show statistically significant elevations or no statistically significant elevations, do not tell us whether any specific health outcome may have been caused by an environmental exposure. The small numbers of outcomes for some rare types of outcomes, which include many types of cancer and birth defects, limit the strength of conclusions that can be drawn from this review.

Because of the shorter latency period for birth outcomes and the multivariate analyses performed to produce birth outcome findings that take account of other risk factors, these findings lend themselves to stronger interpretation than the cancer findings. While some of the low birth weight findings for the exposure group with the highest potential exposures are suggestive of a possible effect of MTBE, the findings were not statistically significant which means no effect was detected.

9.0 RECOMMENDATIONS

We make the following recommendations:

- We recommend this report be shared with Liberty-area residents. We released a draft version of this report in February 2012 for public comment, providing an opportunity for questions and comments. We sent postcards announcing the report's release to area residents who had expressed interest in the past. This final version of the report contains no changes to the report, with the exception of the addition of a summary of the public comments and responses to comments (Appendix C). This final report will be posted on the NYS DOH public website.
- Although the results of this review are not definitive, it is recommended that the investigation's methods and findings be written as a report for a peer-reviewed publication to make the findings available to the scientific community as well as other interested stakeholders.
- There was a statistically significant excess of leukemia among men in the time period 1990-2003, and leukemia is one type of cancer associated with MTBE exposure in animals. Although this is not a cause and effect link and may, in fact, be due to chance or other possible exposures, we recognize this may raise concerns among men and their families. For anyone who is concerned, we recommend they share this information with their health care provider and discuss their concerns. Health Department staff is available as a resource to physicians and community members at 518-402-7950.

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Acknowledgments

This study was supported, in part, by ATSDR and the Centers for Disease Control and Prevention through a Cooperative Agreement Grant to NYS DOH entitled "Program to Conduct and Coordinate Site-specific Activities" (U50/ATU200002), Principal Investigator, Don Miles, Public Health Specialist, Bureau of Environmental Exposure Investigation, Center for Environmental Health, NYSDOH. Our ATSDR Medical and Technical Project Officer is Mohammed Uddin of the Division of Health Studies. Our Technical project officer is Gregory V. Ulirsch, Division of Health Assessment and Consultation. This report was produced independently by NYSDOH and was not reviewed by ATSDR.

Appendix Table 1

Demographics of the Village of Liberty Birth Outcomes Study Area, Sullivan County, New York;
and New York State, excluding New York City: 1990 and 2000

Demographics	1990			2000			1990 ^{1,2}	2000 ^{3,4}
	Liberty	Ferndale	Stevensville	Liberty	Ferndale	Stevensville	New York State, excluding NYC	
Total Population	4,098	308	175	3,873	387	231	10,667,891	10,968,179
Males				46%	55%	45%	49%	49%
Age (years)								
<6	9%	8%	11%	7%	3%	8%	8%	8%
6-19	20%	14%	20%	22%	14%	21%	19%	20%
20-64	52%	53%	57%	54%	57%	56%	59%	58%
>64	19%	24%	11%	17%	25%	15%	13%	14%
Race and ethnicity								
White	83%	85%	88%	76%	83%	85%	90%	85%
Black	12%	11%	6%	14%	13%	2%	7%	8%
Native American	<1%	0%	<1%	<1%	0%	<1%	<1%	<1%
Asian*	2%	2%	4%	2%	<1%	2%	2%	2%
Pacific Islander*				0	<1%	0	<1%	<1%
Other	3%	2%	3%	5%	1%	8%	1%	2%
Multi-Racial**	--	--	--	2%	2%	3%	--	2%
Percent Minority	23%	20%	19%	31%	26%	24%	13%	18%
Percent Hispanic	9%	8%	10%	14%	12%	18%	7%	6%
Income								
Median household income	\$19,317	\$22,361	\$24,999	\$33,786	\$24,411	\$33,152	\$35,711	\$47,517
% below poverty level	18%	5%	6%	18%	30%	7%	9%	10%

* Asian and Pacific Islander categories are combined for 1990 Census.

** Multi-Racial category not available in 1990 Census.

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Appendix Table 2.
Birth Defect Groups Evaluated in the Liberty Study Area

Birth Defect Group	ICD-9 Code	Description	Additional Description
Total Reportable Defects	--	All major structural defects, chromosomal anomalies and metabolic syndromes	All defects reported to the NYS CMR*
Structural Defects	740-759	All major structural defects	Major structural defects comprise the majority of reportable defects
Neural Tube Defects	740.X	Anencephalus – absence of large parts of the brain and skull	The neural tube is the early developmental structure from which the brain and spinal cord develop.
	741.X	Spina bifida – the spinal column is not completely formed	
	742.0X	Encephalocele – part of the brain comes through opening(s) in the skull	
Total Cardiac Defects	745.0-747.9	All cardiac defects <i>excluding</i> patent ductus arteriosus (747.0) in children weighing less than 2500g at birth	All heart defects
Major Cardiac Defects	745.0	Common truncus	Major heart defects There is a complex sequence of events that result in a well formed heart at birth and disruption of any portion may result in a defect.
	745.1	Transposition of great vessels	
	745.2	Tetralogy of Fallot	
	746.0	Anomalies of pulmonary valve	
	746.1	Tricuspid atresia and stenosis	
	746.3	Congenital stenosis of aortic arch	
	746.4	Congenital insufficiency of aortic valve	
	746.7	Hypoplastic left heart syndrome	
Cleft lip/cleft palate	749.00-749.04	Cleft palate	The two plates of the skull that form the roof of the mouth are not completely joined. Facial tissues are not completely joined, appearing as a gap or indentation of the top lip or between the lip and nose.
	749.10-749.14	Cleft lip	
	749.20-749.25	Cleft palate with cleft lip	
Choanal atresia	748.00	Choanal atresia	Defect of nasal airway

Abbreviations: X = 0 through 9

See the NYS DOH Congenital Malformation Registry Handbook for more information (NYS DOH, 2006).

Appendix Table 3

**BUREAU OF CANCER EPIDEMIOLOGY
NEW YORK STATE DEPARTMENT OF HEALTH**

Observed and Expected Numbers of Incident Cancer Cases,
ZIP Codes 12754 and 12768
Sullivan County, New York, 1980-1989
New York State exclusive of New York City Standard 1980-1989

SITES (ICD-O-2) ^a	MALES					FEMALES				
	# cases		SIR	95% C.I.		# cases		SIR	95% CI	
	Ob- served	Ex- pected		Lower	Upper	Ob- served	Ex- pected		Lower	Upper
All Sites ^d	227	233	0.97	0.85	1.11	221	222	1.00	0.87	1.14
Oral Cavity / Pharynx	8	8	1.06	0.46	2.08	– ^e	4	– ^e	– ^e	– ^e
Esophagus	– ^e	3	– ^e	– ^e	– ^e	– ^e	1	– ^e	– ^e	– ^e
Stomach	– ^e	7	– ^e	– ^e	– ^e	– ^e	4	– ^e	– ^e	– ^e
Colorectal	39	38	1.03	0.73	1.41	44	37	1.18	0.86	1.58
Liver / Intrahepatic Bile Duct	– ^e	2	– ^e	– ^e	– ^e	– ^e	1	– ^e	– ^e	– ^e
Pancreas	– ^e	7	– ^e	– ^e	– ^e	– ^e	7	– ^e	– ^e	– ^e
Larynx	7	5	1.40	0.56	2.88	– ^e	1	– ^e	– ^e	– ^e
Lung / Bronchus	58	48	1.20	0.91	1.55	31	24	1.29	0.87	1.83
Female Breast						51	60	0.84	0.63	1.11
Cervix uteri						7	5	1.49	0.60	3.08
Corpus Uterus / Uterus (not otherwise specified)						10	14	0.73	0.35	1.35
Ovary						7	9	0.77	0.31	1.58
Prostate	39	43	0.91	0.64	1.24					
Testis	– ^e	2	– ^e	– ^e	– ^e					
Urinary Bladder (including in situ)	16	19	0.85	0.49	1.38	– ^e	7	– ^e	– ^e	– ^e
Kidney / Renal Pelvis	– ^e	6	– ^e	– ^e	– ^e	0	4	0.00	0.00	0.81
Brain / Other Nervous System	– ^e	4	– ^e	– ^e	– ^e	– ^e	3	– ^e	– ^e	– ^e
Thyroid	– ^e	1	– ^e	– ^e	– ^e	– ^e	2	– ^e	– ^e	– ^e
Lymphomas	7	9	0.74	0.30	1.52	10	8	1.17	0.56	2.16
Multiple Myeloma	– ^e	3	– ^e	– ^e	– ^e	– ^e	3	– ^e	– ^e	– ^e
Leukemias	– ^e	7	– ^e	– ^e	– ^e	7	6	1.22	0.49	2.52

^aClassification of site is based on ICD for Oncology, 2nd Edition (Percy et al. 1990)

^bData were obtained from the New York State Cancer Registry (database as of March 2006).

^cExpected numbers are based on 1989 standard using estimates from 1980 Geolytics and 1990 Claritas population data. Total populations: 42,334 males and 43,495 females.

^dIncludes observed and expected numbers of cases at sites of cancer not listed below.

^eThe number of cases is not shown to protect patient confidentiality.

*The number of cases observed is significantly different from the number expected based on statistical testing against the Poisson distribution at a significance level (two-tailed) of 0.05.

Appendix A

Methods for geocoding births

We obtained the residential address for all births within ZIP Codes 12734, 12754, 12768 and 12783 which contain the entire study area. To capture records with incorrect or missing ZIP Codes, we also obtained the addresses for all birth records in Sullivan County without a ZIP Code. The addresses were put into the U.S. Postal Service standard format, and using commercially available geographic information system (GIS) software, the addresses were assigned geographic coordinates (latitude and longitude) (Mapinfo, 2007). When a street name could not be matched using the GIS software, the accuracy of the location was inadequate or for records with incomplete addresses that could not be geocoded, we also looked for addresses using search engines, street maps, city directories, and NYS Department of Motor Vehicle records. After the geographic coordinates were assigned to the records, the locations were overlaid onto digital maps of the study area. The records falling inside the study area boundary (the water district boundaries) were then “captured” and classified as exposed. To protect confidentiality, no maps of individual case locations are reported.

A total of 3,239 birth records from ZIP Codes 12734, 12754, 12768 and 12783 were selected for geocoding to determine if the mothers resided in the study area at the time of birth. Birth records in Sullivan County with no ZIP Code were also selected. 88% of the residential addresses were geocoded to the degree of accuracy necessary to determine whether or not they were inside the study area boundary. The addresses that could not be geocoded were primarily PO boxes, rural routes, or very old addresses from the late 1970s without a house number. This process resulted in 1,724 birth records being assigned to the exposed group (i.e., in the study area).

Appendix B

Other types of cancer associated with MTBE exposure in animals

Cancer of the Liver/Intrahepatic Bile Duct There were eight cases of cancer of the liver and intrahepatic duct diagnosed among men residing in the study area, while four cases were expected. The number observed was higher than expected but it was not statistically significant. Among females, fewer than six cases were diagnosed while two were expected. (To protect patient confidentiality, an exact number cannot be provided when there are fewer than six observed cases.) Since this cancer is associated with MTBE exposure in animals and the number of cases diagnosed among males was high compared to the number expected, the cases were examined in more detail.

Cancer of the liver and intrahepatic bile duct is more common in older people. In New York State over half of newly diagnosed patients are age 65 and older. The ages of the males in the study area diagnosed with this cancer ranged, in years, from the early 40s to the elderly. Half of these men were diagnosed after the age of 65. When 10-year age groups were examined separately, a statistically significant excess was found in the 45-54 year age group, though it should be noted that the number of cases was small. No more than two men were diagnosed in any given year during the time period of the study. A majority of the men were diagnosed after 1995.

The residence at the time of diagnosis of each of the males and females was also examined to determine whether there was any geographic clustering of cases. The residence was marked on a street map of the study area. Residences of the individuals were found to be scattered throughout the study area with most of them located in the Village reflecting the distribution of the population. Plotting the residential addresses on a map did not show any evidence of unusual geographic distribution.

Primary liver cancer is rare, but the liver is a frequent site of metastasis for other cancers, and liver cancer can be misreported especially if the death certificate was the only source of information. Of the eight males diagnosed with liver cancer, information from the Cancer Registry indicated that five were microscopically confirmed, two were unconfirmed and one had a death certificate as the only reporting source. Medical records for the males and females were requested to obtain additional information and to confirm the diagnosis. Records were received for five of the eight males (62%) and for all of the females. The diagnosis of the cancer was confirmed for these individuals as well as the address at the time of diagnosis. One of the females originally identified for this study was found to reside outside of the study area and was therefore not included in the study.

Scientists do not know exactly what causes this cancer. There are several different types of liver cancer with the most common associated with long-term excessive alcohol consumption, cirrhosis, and hepatitis B virus or hepatitis C virus infection. Long-term use of anabolic steroids can also increase the risk of getting this cancer. Studies have also shown that workers exposed to vinyl chloride during the manufacturing of some plastics have an increased risk of getting liver cancer. (Struver et al., 2002) After reviewing the medical records, it was found that a majority of the five males had at least one of the above risk factors for getting liver cancer.

Cancer of the Kidney/Renal Pelvis: Seven cases of cancer of the kidney and renal pelvis were diagnosed among men residing in the study area, while ten cases were expected. Among females, fewer than six

cases were diagnosed while seven were expected. The numbers of cases were less than expected for both males and females in the study area, with neither being statistically significantly different.

Cancer of the kidney and renal pelvis is more common in older people and in men. The risk of getting this cancer increases with age, most often occurring in people over the age of 50. Scientists do not know exactly what causes this cancer. Some types of kidney cancer are more common in people with certain rare genetic disorders (von Hippel-Lindau disease and some others) and in people with a family history of kidney cancer. It is also more common in urban, industrialized areas. Research also suggests that people who smoke are twice as likely to develop this cancer as non-smokers. Coke oven workers in steel plants and workers exposed to asbestos or cadmium may also have an increased risk. Other studies indicate that radiation therapy for disorders of the uterus, exposure to thorotrast (a radioactive substance used in the 1920s), and heavy and long-term use of the drug phenacetin (a pain killer no longer used in the US) may also be associated with this cancer. (Lindblad et al., 2002)

The residence at the time of diagnosis of each of the males and females diagnosed with cancer of the kidney and renal pelvis was marked on a street map of the study area to look for any geographic clustering of cases. Two of the residences could not be plotted due to insufficient street address information. The residences that could be plotted were scattered in and around the Village. Plotting the residential addresses on a map did not show any evidence of unusual geographic distribution, although some individuals were residents in apartment buildings and senior citizen housing.

Cancer of the Testis: Fewer than six cases of testicular cancer were observed among men residing in the study area, while approximately three cases were expected. The number of cases observed was not statistically significantly different from the number expected.

Incidence of this cancer has doubled in the past twenty years, with most of the increase being among young men aged 15 to 44 years. In the US, the incidence of testicular cancer is six times higher among white males than African-American males. It is the most common cancer among white males aged 20 to 34 years and the second most common cancer among white males aged 15 to 19 and 35 to 39 years.

It is not known exactly what causes testicular cancer. We do know that testicular cancer occurs more often in men with certain medical conditions, including undescended testis. Research also indicates that men in white-collar or professional occupations are at a higher risk, suggesting that socioeconomic status or lifestyle may be linked to risk factors for this cancer. Employment in the military, aviation equipment support, crude petroleum and natural gas extraction, printing and leather finishing industries has been associated with cancer of the testis. (Tamimi et al., 2002)

The residence at the time of diagnosis of each of the males diagnosed with testicular cancer was marked on a street map of the study area. None of the small number of these men lived in the Village. Plotting the residential addresses on a map did not show any evidence of unusual geographic distribution.

Lymphomas: Sixteen cases of lymphoma were diagnosed among men residing in the study area, while 15 cases were expected. Among females, 17 cases were diagnosed while 15 were expected. The number of cases observed was not statistically significantly different from the number expected for males and females separately.

Lymphomas are often divided into two groups: non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (Hodgkin's disease). Non-Hodgkin's lymphoma occurs more frequently than Hodgkin's disease. Both occur more frequently in men than in women. Although both can occur in children and adults, approximately 70% of people diagnosed with NHL are age 50 or older. Hodgkin's disease is more common in early adulthood (age 25 to 30) and late adulthood (after age 55). About 10-15% of cases are diagnosed in children 16 years of age and younger.

A majority of the men and women diagnosed with lymphoma in the study area were diagnosed with NHL. Seventy-five percent of these individuals were over the age of 50. A much smaller number of individuals with Hodgkin's disease were diagnosed in the study area. Most of these individuals were under the age of 25.

One of the risk factors associated with lymphoma is a compromised immune system. Those who have had organ transplants and individuals with HIV/AIDS have an increased risk of developing NHL. There is an increased risk of Hodgkin's disease in people who have had infectious mononucleosis (an infection caused by the Epstein-Barr virus). Research studies also suggest that exposure to herbicides, pesticides and certain other chemicals may be associated with the development of NHL. (Melbye et al., 2002a; Melbye et al., 2002b)

The residence at the time of diagnosis of each of the males and females diagnosed with lymphoma was marked on a street map of the study area. Two of the addresses (one male and one female) could not be plotted due to insufficient street address information while two of the addresses of the males had to be approximated for the same reason. Most of the individuals resided in and around the village. Plotting the residential addresses on a map did not show any evidence of unusual geographic distribution, although some individuals were residents in apartment buildings, senior citizen housing and other facilities.

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Appendix C
Summary of Public Comments and Responses

This summary was prepared to address comments and questions on the public comment draft of the Health Statistics Review for the Village of Liberty that was released on February 29, 2012. The public was invited to review the draft during the public comment period which ran through March 30, 2012. We solicited comments on the draft report to understand remaining community concerns and questions. We received verbal and written comments from two individuals during the comment period. The contents of the two comments were very similar. We summarize the comments below and provide a written response.

Comment. Why didn't the researchers investigate the possible effect of MTBE on neurological outcomes such as multiple sclerosis (MS) and/or attention deficit and hyperactivity disorders (ADD/ADHD)? Do you plan to include these outcomes in a future investigation?

We did not include neurological outcomes in this investigation because we do not have access to high quality, comprehensive data on the incidence or prevalence of these conditions in specific geographic areas of NYS. The investigation included outcomes for which we have very complete, diagnostically specific, individual-level data from birth certificates, the NYS Cancer Registry and the NYS Congenital Malformations Registry. Unfortunately, at this time, we are not able to acquire the similarly complete data for neurological outcomes that would be needed for this type of health outcomes review. We have no plans to investigate any additional health outcomes in the Village of Liberty at this time.