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Center for Environmental Health

PUBLIC COMMENT DRAFT

Public Health Consultation

**Health Statistics Review:
Birth Outcomes and Cancer**

**Hopewell Precision Contamination Site,
Hamlet of Hopewell Junction, Town of East Fishkill
Dutchess County, New York**

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Prepared by:

The New York State Department of Health
Center for Environmental Health
Troy, New York

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

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EXECUTIVE SUMMARY

Health Statistics Review of Cancer and Birth Outcomes, Hopewell Precision Contamination Site, Hamlet of Hopewell Junction, Dutchess County, New York

Background

The New York State Department of Health (NYS DOH) conducted this health statistics review because of concerns about environmental health issues related to the Hopewell Precision Contamination Site in the Hamlet of Hopewell Junction, Dutchess County, New York. This type of review looks at levels of health outcomes among the population of a specific geographic area and provides residents with information about numbers of outcomes in their area compared with expected numbers based on statewide data. This type of review can not link cause (exposure) and effect (health outcome) and cannot prove that an individual's health problem was caused by an environmental exposure from this site.

As a result of activities at the Hopewell Precision facility, groundwater in the area is contaminated with volatile organic compounds (VOCs), primarily trichloroethene (TCE) and 1,1,1-trichloroethane (1,1,1-TCA). Some residents in this area were exposed to VOCs via drinking water from private wells and contaminated indoor air through a pathway known as soil vapor intrusion. This study, which reviews health outcome data routinely collected by NYS, is intended to address some of the community's environmental health concerns related to the Hopewell Precision Contamination Site.

Because some studies have found that VOC exposures are associated with several types of cancer and reproductive effects, this health statistics review focuses on these outcomes, including low birth weight and prematurity, birth defects, and cancer. This type of review is feasible because NYS DOH collects comprehensive data on these health outcomes for all NYS residents. While there are other health effects of interest potentially associated with VOC exposures (for example, autoimmune or neurological outcomes), incorporating these outcomes in this health statistics review is not feasible because comprehensive statewide data are not available for these outcomes.

NYS DOH is in the process of combining health outcome data from several small populations with exposures similar to those in the Hopewell Precision study area to create a larger population for evaluating birth outcomes and cancer in a combined health statistics review. NYS DOH is planning to include the Hopewell Precision study area in this combined review. The separate review presented in this report was requested by residents of Hopewell Junction. Residents were advised in advance that the small population and small numbers of observed outcomes would limit the ability of this health statistics review to draw strong conclusions about levels of health outcomes in the Hopewell Precision area.

Health Statistics Review Objective

The objective of this review is to evaluate the levels of adverse birth outcomes and cancer in the study area compared to NYS (excluding New York City [NYC]) and determine if the levels of these health outcomes are higher, lower, or about the same as what would be expected given the population of the Hopewell Precision study area.

Methods

The boundaries of the health statistics review study area were selected by identifying the U.S. Census blocks that include the Hopewell Precision groundwater contamination plume. Study area boundaries were presented to members of the community for their input and to ensure that the study area included the population with the highest probability of exposure.

NYS DOH reviewed birth outcomes and cancer outcomes occurring in the study area through 2005. The first year of available data determined the beginning of the study timeframe. 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 1978-2005. All reportable birth defects were evaluated for 1983-2005. Cancer diagnoses for all types of cancer combined and ten specific anatomical sites were evaluated for 1980-2005. For all outcomes, the expected numbers were calculated using rates for NYS excluding NYC. In addition, for the birth outcomes (low birth weight, prematurity, growth restriction and sex ratio), logistic 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, baby's gender, and year of birth.

Results and Discussion

The birth outcomes review showed that the numbers of premature births and male births (sex ratio) in the Hopewell study area were similar to expected numbers. The low birth weight and growth restriction outcome categories, which largely overlap, all showed deficits (fewer than expected numbers), but only the small for gestational age category showed a statistically significant deficit. The number of birth defects in the study area was similar to the number expected. There was no evidence of elevations of major heart defects or cleft palate, birth defects found in excess in other studies of VOC exposures. The pattern of specific types of birth defects did not appear to be unusual.

The total number of cancers diagnosed among residents of the study area was similar to the number expected and no specific type of cancer showed a statistically significant excess or deficit. This review found no excesses of lymphoma or kidney cancer, two types of cancer associated with VOC exposure in other studies. Esophageal cancer, associated with VOC exposures in some studies, was elevated in the study area, but the elevation was not statistically significant.

The small population size and small number of observed outcomes limit this review's ability to detect excesses in health outcomes and meaningful patterns for most types of birth outcomes and

specific types of cancer. Additional limitations include the lack of complete information about the levels of VOCs in individual homes, the duration of the exposure, the amount of time residents spent in the home each day, the possibility of other exposure pathways, or additional exposures. In addition, this type of review cannot take into account personal information that may be related to the health outcomes, such as medical history, dietary and lifestyle choices (e.g., smoking and drinking), and occupational exposures to other chemicals.

Recommendations

With the limitations of this review in mind, NYS DOH and the Agency for Toxic Substances and Disease Registry (ATSDR) make the following recommendations for next steps:

1. Include the Hopewell Precision study area in the combined health statistics review currently being conducted for several other smaller sites in NYS with similar VOC exposures. The larger combined review may be able to draw stronger conclusions than this review because there will be a larger population, with higher numbers of birth outcomes, birth defects, and cancers expected.
2. Work with area residents to address additional health concerns not included in this review. This effort includes learning more details from the community about other types of health concerns and addressing such concerns by developing a follow-up plan jointly with interested residents. This process may involve working with other agencies, consulting additional experts, and further study, if feasible.

1.0 INTRODUCTION

The New York State Department of Health (NYS DOH) has a cooperative agreement with the Agency for Toxic Substances and Disease Registry (ATSDR) to conduct public health assessments in NYS communities which may have been impacted by environmental contamination. In September 2007, a Public Health Assessment (PHA) evaluating human exposure pathways for contaminants related to the Hopewell Precision Contamination Site was released (ATSDR, 2007). More detailed information about the site description and history, exposure investigation, actions implemented during the public health assessment process, and the Public Health Action Plan for the site can be found in the PHA.

As one component of the Public Health Action Plan, NYS DOH agreed to conduct a health statistics review for the area. A health statistics review is a descriptive epidemiologic study that analyzes existing health information (such as birth and death records, disease registries, or hospital admissions) to compare rates of health outcomes in a local community to national, statewide, or other reference population rates. The purpose of this investigation is to evaluate the levels of health outcomes in the area affected by VOC contamination from the Hopewell Precision Contamination site. While this health statistics review cannot prove that VOC contamination from the Hopewell Precision Contamination site is causing cancer or birth outcomes in the area, it can generate hypotheses and may indicate whether further detailed health investigations are warranted.

2.0 BACKGROUND

2.1 Hopewell Precision Contamination Site exposure history

The brief information provided in this section is from the ATSDR PHA of the Hopewell Precision Contamination Site (ATSDR, 2007). Additional details about the site and nearby population, including sampling data and information about estimates of health risks associated with exposure, can be found in the 2007 PHA. The site is located in a semi-rural residential area of Dutchess County, New York. Hopewell Precision is an active manufacturer that fabricates and paints sheet metal. The facility, which opened in 1977, originally operated at 15 Ryan Drive but moved its operations to 19 Ryan Drive in 1981. The combined size of these two adjacent properties is 5.7 acres. Waste products from the Hopewell Precision Contamination site include paint thinners and degreasing solvents. Mishandling of these waste products, including dumping five-gallon buckets containing these wastes on the ground outside the back door, allegedly occurred at the original location (15 Ryan Drive). As a result, area groundwater is contaminated with volatile organic compounds (VOCs), primarily trichloroethene (TCE) and 1,1,1-trichloroethane (1,1,1-TCA). Area soil vapor has also been impacted as a result of the VOC groundwater plume. Exposures to TCE and 1,1,1-TCA from drinking water and indoor air have occurred via private drinking water wells and soil vapor intrusion.

The area impacted by the groundwater and soil vapor contamination extends approximately 1.4 miles in a southwestern direction from the Hopewell Precision Contamination site, generally

following NYS Route 82. About 700 people lived in the affected area in 1980. All residents in the affected area rely on private wells as their primary source of potable water. Impacted wells in the study area are contaminated with VOCs, primarily TCE and to a lesser extent 1,1,1-TCA. TCE is the primary site-related soil vapor contaminant.

For the Hopewell Precision Contamination site, there are two known completed site-related exposure pathways (or the manner in which the VOCs actually enter the body): exposure to TCE (primarily) and 1,1,1-TCA in private drinking water and contaminated soil vapor intruding into indoor air. Exposure to contaminants in drinking water supplies can occur through ingestion, dermal contact, and absorption during showering, bathing, or other household water uses, and through inhalation of aerosols and vapors from water used in the household. Indoor air can become contaminated when vapors beneath a building are drawn through cracks and openings in the foundation. Exposure to contaminants in indoor air can occur through inhalation.

For an undetermined period of time some residents were exposed to VOCs in their drinking water supply and/or indoor air. Prior to well water sampling in February 2003, we do not know how long or at what concentration residents were exposed to site-related contaminants in their drinking water. However, limited sampling of private wells in 1985 showed no contamination. Prior to soil vapor and indoor air sampling in February 2004, we do not know for how long or to what concentration residents were exposed to site-related contaminants in their indoor air. The maximum duration for both the drinking water and vapor intrusion exposure pathways could be as long as 29 years for some of the homes in the contamination area, because some of these homes were built and the potential source facility was operational as early as 1977. However, it is quite likely that the movement of the contamination to groundwater, private drinking water wells, and soil vapor could have taken a long time, resulting in shorter exposure duration.

Although these pathways were complete in the past, most exposures were eliminated or minimized after contamination was identified. Treatment systems were installed on drinking water wells where VOCs were detected at or above the NYS public drinking water standard (5 micrograms per liter) and sub-slab depressurization systems were installed at homes where soil vapor intrusion was occurring or could occur. One property owner refused the installation of the treatment systems on the property and therefore, exposures may be currently occurring. Additional exposures to these contaminants above standards or guidelines could occur if treatment systems are not maintained, TCE or 1,1,1-TCA are detected at or above the State standard in any wells where contamination was not previously identified, or TCE is detected in sub-slab vapor in any additional buildings.

2.2 VOC exposures and potential health risks

For an undetermined period of time, possibly for up to 29 years, some of the private water supply wells near the Hopewell Precision Contamination site were contaminated with TCE and 1,1,1-TCA. Some private wells also contained methyl tert-butyl ether (MTBE), which is not considered related to the Hopewell Precision facility. Some concentrations of TCE, 1,1,1-TCA and MTBE detected in private wells were higher than the NYS public drinking water standard

and/or PHA comparison values. Therefore, these chemicals were selected for further evaluation of potential health outcomes.

Trichloroethene (TCE)

In humans, long-term exposure in the workplace to high levels of TCE in air is linked to effects on the central nervous system and irritation of the mucous membranes. Some studies of people exposed to high levels of TCE in workplace air or in drinking water show an association between exposure to TCE and increased risks for certain types of cancer, including cancers of the kidney, liver, esophagus, and non-Hodgkin's lymphoma. Other studies suggest an association between workplace TCE exposure and reproductive effects (alterations in sperm counts) in men.

Studies of women exposed to mixtures of chlorinated solvents (including TCE) in drinking water during pregnancy also suggest TCE may increase the risk of birth defects (e.g., neural tube defects, oral cleft defects, and congenital heart defects) and/or childhood leukemia (ATSDR, 1997a). In each of the drinking water studies, however, there are uncertainties about how much contaminated water the women drank during pregnancy and about how much TCE was in the water the women drank while pregnant. In addition, we do not know if the health effects observed in the studies of human exposure to TCE in workplace air and in drinking water are due to TCE or other factors, including exposure to other chemicals, smoking, alcohol consumption, and lifestyle choices. Since these potential confounding factors were not well controlled, and because there were uncertainties about actual exposures, the studies in humans suggest, but do not prove, that exposure to TCE can cause cancer, developmental effects, and reproductive effects in humans.

In animal studies, exposure to high levels of TCE caused adverse effects on the central nervous system, liver, and kidneys. Lifetime exposure to high levels of TCE has caused cancer in laboratory animals. When pregnant animals were exposed by ingestion to large amounts of TCE, adverse effects on the normal development of the offspring were observed (ATSDR 1997b). In most, but not all of these studies, the high amounts of the chemicals also caused adverse health effects on the parent animals. In one set of studies, effects on fetal heart development were observed in the offspring of rats exposed to TCE in drinking water before and during pregnancy (Dawson, 1993; Johnson, 1998; Johnson, 2003).

1,1,1-Trichloroethane (1,1,1-TCA)

Exposure to high levels of 1,1,1-TCA can cause adverse effects on the nervous system, liver, and cardiovascular system (ATSDR, 1995). These effects have also been observed in laboratory animals exposed to high levels of 1,1,1-TCA. Available toxicological data are inadequate to assess the carcinogenic potential of 1,1,1-TCA (US EPA IRIS, 2004).

Methyl-tert-Butyl Ether (MTBE)

Studies with laboratory animals show that exposure to very high levels of MTBE affected the central nervous system, gastrointestinal tract, kidney, liver, and blood. Studies on pregnant rats and mice show that exposure to very high levels of MTBE altered the normal development of fetal and young rodents, but only at exposure levels that harmed the adult animals. Studies in laboratory animals that breathed or ingested high levels of MTBE over their lifetimes showed a

slight increase in tumors. Whether exposure to MTBE causes tumors in humans is unknown. (Bird, 1997; Belpoggi, 1995; 1998).

2.3 Health outcomes included in this health statistics review

Because VOC exposures have been associated with reproductive effects and cancer, this health statistics review focuses on these outcomes. This type of review is feasible because NYS DOH collects comprehensive data on cancer and birth outcomes for the NYS population. While there are other health effects of interest potentially associated with VOC exposures (for example, autoimmune or neurological outcomes), including these health effects in this health statistics review is not feasible because comprehensive statewide data are not available.

Low birth weight

Cigarette smoking is the single largest risk factor for fetal growth restriction and low birth weight in non-premature infants (Kramer, 1987). Studies have also found a persistent association between low birth weight and measures of socioeconomic status, including occupation, income, and education (Hughes and Simpson, 1995). Poverty can be associated with reduced access to health care, poor nutrition, and an increased risk of behavioral risk factors such as smoking. Poor nutritional status of the mother at conception and inadequate nutritional intake during pregnancy can result in term low birth weight births (Kramer, 1987). Although mother's education is not a direct measure of socioeconomic status, birth certificates contain information about mother's education that is often used as an indicator for a variety of low socio-economic status risk factors.

Small for gestational age

There are various reasons that babies might be born underweight for their gestational age (small for gestational age), including restricted fetal growth during pregnancy or smaller than average size parents. Small for gestational age babies can have low birth weight because something slowed or halted their growth in the uterus (Robinson, 2000). Small for gestational age births are an important health outcome because babies who are small for gestational age are more likely to have health problems as newborns and children.

Maternal cigarette smoking is a major risk factor for having a small for gestational age baby. In fact, a 2004 report from the Surgeon General indicates that there is sufficient evidence to infer a cause and effect relationship between maternal smoking and fetal growth restriction and low birth weight (USDHHS, 2004). When expectant mothers have poor nutrition, smoke, or use alcohol or illegal drugs, their babies have an increased chance of being small for gestational age (Resnick, 2002).

Other factors also influence the risk of having a small for gestational age baby. If a baby has birth defects, is a twin or triplet, has fetal infections or has an abnormality of the placenta, the baby's chances of being small for gestational age may increase. Maternal diseases or medical conditions that reduce the blood flow to the fetus may account for 25 – 30 percent of small for gestational age births (Resnick, 2002). Health care provider visits before becoming pregnant and

during pregnancy are helpful for identifying and controlling these medical conditions (NYS DOH, 2006a). Prenatal care is also essential for determining whether a baby is growing normally. In some cases, fetal growth can be improved by treating any medical condition in the mother (such as high blood pressure) that may be a contributing factor (March of Dimes, 2005).

Preterm birth

Preterm birth babies are born before 37 weeks gestation. Preterm birth is an important health outcome because it causes the greatest risk for infant mortality (death before one year of age). Unfortunately, little is known about the specific causes of preterm birth. Significant differences exist among groups, with African-American women having a greater risk than white women for preterm delivery, even in studies that control for socio-economic differences. Visits to a healthcare provider before pregnancy and seeking early and regular prenatal care may help reduce the risk of delivering a baby preterm (March of Dimes, 2004).

Birth defects

While scientists have been able to identify some causes of specific birth defects, the cause of most birth defects is unknown. In fact, about 40 – 60 percent of birth defects are of unknown origin (Kalter, 1983). Genetic and environmental factors can cause birth defects. Twenty percent of birth defects may be due to a combination of heredity and other factors, eight percent to single gene mutations, six percent to chromosomal abnormalities, and five percent to maternal illnesses, such as diabetes, infections, or anticonvulsant drugs (Kalter, 1983; Nelson, 1989). Radiation exposure and the use of certain drugs, such as thalidomide or Accutane, are associated with birth defects. Women who smoke, use alcohol or illegal drugs while pregnant have a higher risk of having a baby with a birth defect.

There are ways to reduce a baby's risk for birth defects and to ensure early treatment if a birth defect is found. Pre-pregnancy visits with health care providers may identify genetic or other maternal health conditions which can be treated. A woman's daily use of a multivitamin with 400 micrograms of the B vitamin, folic acid, before and during pregnancy, also helps prevent some types of birth defects (Eichholzer, 2006). Women are advised to talk to their health care providers about any medications they take and refrain from smoking, drinking alcohol, or taking illegal drugs while trying to become pregnant or during pregnancy (NYS DOH, 2006a). Despite all of these efforts, birth defects may still occur. To improve health outcomes, certain medical screenings during pregnancy may assist early identification of any birth defects and lead to early infant treatment.

No consistent pattern has been observed for associations between either race, ethnicity, or socioeconomic status, and the risk of birth defects as a group or for heart defects specifically. A recent case-control study by Carmichael, et al. (2003) found an increased risk of transposition of the great arteries associated with low socioeconomic status (SES), but a reduced risk of tetralogy of Fallot associated with low SES. However, the number of infants in each group was small and none of the results were statistically significant. Several studies have found no association between SES and all heart defects combined (Botto, 1996; Correa-Villasenor, 1991; Heinonen, 1976). While a large British study reported a positive association between all heart defects

combined and lower socioeconomic deprivation scores, the association was not statistically significant (Vrijheid, 2000). The same study did report a significant association between defects of the cardiac septa and lower socioeconomic deprivation; however, other cardiac defects examined were not significantly elevated. The Baltimore Washington Infant Study, one of the largest birth defects studies in this country, found that the relationship between SES and heart defects varied by type of defect examined (Ferencz, 1997; Correa-Villasenor, 1991).

Sex ratio

An additional outcome available from birth data evaluated in this review is the ratio of male to female births. While there are no studies of the effects of TCE, PCE, or VOCs in general on sex ratios in humans, some studies of other environmental exposures have shown effects on sex ratios. Studies of sex ratios and occupational and environmental exposures have found a decrease in the number and proportion of male births for exposures to dioxins (Mocarelli, 1996), DDT (Cocco, 2005), the nematocide dibromochloropropane (DBCP) (Goldsmith, 1984), hexachlorobenzene (Jarrell, 2002) and certain heavy metals (Sakamoto, 2001; Figa-Talamanca and Petrelli, 2000). For the most part, these chemicals are unlike VOCs in that they tend to be persistent in the environment and bio-accumulate in the body following exposure. The exact biological mechanism by which environmental exposures may alter sex ratios is unknown, but it is thought to involve endocrine (hormonal) disruption in either parent.

Cancer

A review of cancer risk factors for all types of cancer is beyond the scope of this report because cancer is not a single disease, but more than 100 different diseases. Cancer is characterized by the abnormal growth of cells in the body. Cancer types are usually labeled based on the type of cell that has grown abnormally to form a tumor. A tumor is malignant, or cancerous, if it is able to spread to other tissues or organs in the body.

Generally, each type of cancer has its own spectrum of risk factors, symptoms, outlook for cure, and methods of treatment. A family history of cancer is a strong risk factor. There are some known carcinogens that increase risk for more than one type of cancer, such as X-rays and tobacco. Other carcinogens include sunlight and certain chemicals that may be found in the air, water, food, drugs, and workplace. Personal habits, lifestyle, and diet may contribute to many cancers. It is estimated that about 30 percent of cancer deaths are due to tobacco. Most types of cancer develop slowly in people. They may appear from five to 40 years after exposure to a carcinogen. For example, cancer of the lung may not occur until 30 years after a person starts smoking. This long latency period is one of the reasons it is difficult to determine what causes cancer in humans (NYS DOH 2006b).

2.4 Objective

The objective of this review is to evaluate the levels of adverse birth outcomes and cancer in the study area compared to NYS (excluding NYC) and determine if the levels of these health outcomes are higher, lower, or about the same as what would be expected given the population of the Hopewell Precision study area.

3.0 METHODS

3.1 Study design

This study uses a geographically-based ecological study design to determine if incidence of adverse health outcomes in the Hopewell Precision study area are different from NYS, excluding NYC. Birth outcome analyses were adjusted for the age, race, and education of the mother, the year of birth, prenatal care, the number previous births (parity), and the gender of the infant. Cancer analyses are adjusted for age, gender, and year of diagnosis. The boundaries of the health statistics review study area were selected by identifying the U.S. Census blocks that include the Hopewell Precision groundwater contamination plume. The population in the study area and the births to women living in the study area are considered potentially exposed to VOCs. All analyses were performed using SAS version 9.1 (SAS Institute Inc., 2003). Statistical terms are defined in the glossary (see section 7.0).

3.2 Selection of study area boundaries

The location of the contaminant plume was provided on a digital map of Hopewell Junction and another digital map of the 2000 U.S. Census block boundaries was then overlaid. Eight Census blocks that encompass the majority of residences located above the contaminant plume were selected (Figure 1). Study area boundaries were presented to members of the community to ensure that study area boundary decisions incorporated their input and included the population with the highest probability of exposures. Information from the community is especially important because decisions about study boundaries usually require some trade-offs. Census boundaries are needed for estimating the population of the study area, but they usually do not coincide well with the boundaries associated with potential exposures. Therefore, this frequently results in the inclusion of some population that is known not to have been exposed. A meeting was held in April 2007 to discuss the boundaries, and an information sheet with the proposed boundaries was mailed to area residents in May 2007.

3.3 Demographic characteristics of the study area and comparison populations

Table 1 compares the demographic characteristics of the population of the study area to the population of NYS (excluding NYC). In 2000, the population of the study area was 858 persons. The population of the study area increased by 3 percent between 1980 and 1990 and increased by 19 percent between 1990 and 2000, for an overall increase of 22 percent. The population of the State (excluding NYC) increased by only five percent over the same time period. The age distribution of the study area is similar to that of the State. The study area population was 98 percent white in 2000 compared to 85 percent white for the State (excluding NYC). The study area and the State were both six percent Hispanic in 2000. The study area's median income is considerably higher than the median income of NYS (excluding NYC). In 1980, the study area median income was 22 percent higher than statewide, 70 percent higher in 1990, and 57 percent

higher in 2000. The most recent 2000 data estimates study area median income as \$74,712 compared to the statewide median income of \$47,517.

3.4 Birth outcomes

NYS DOH used birth certificate data for 1978-2005 (28 years) to determine if the study area had an increased number of adverse birth outcomes or unusual patterns. Only singleton births (one baby) were included in this study because multiple births (e.g., twins, triplets) have a much higher risk of some adverse birth outcomes. NYS DOH identified all singleton births to mothers living in the study area by placing the mother's address from the birth certificate on a map (see section 3.7). Birth certificates for all singleton births during the same years to mothers living in NYS (excluding NYC) were used for comparison. The birth certificate data include the infant's birth weight, gestational age, and gender. In addition, information is available on the mother's age, race, ethnicity, years of education, the number of previous births (parity), and the week of pregnancy when she had her first prenatal visit.

Birth outcomes are divided into four groups: birth weight, prematurity, growth restriction, and male to female ratio. The birth weight outcomes are: low birth weight (LBW) (<2500 g), moderately LBW (≥ 1500 g and <2500g), and very LBW (<1500g). Birth records with missing birth weight or birth weight outside a reasonable range (<100g or >8000g) were excluded from the analysis. The prematurity outcomes are: pre-term births (<37 weeks gestation), moderately pre-term births (≥ 32 and <37 weeks gestation), and very pre-term births (<32 weeks gestation). Birth records missing gestational age or with gestational ages outside the reasonable range (<20 weeks or >44 weeks) were excluded from the analysis. Two measures of growth restriction were studied: small for gestational age (SGA) births and term LBW. SGA is defined as a birth weight below the 10th percentile of the NYS (excluding NYC) birth weight distribution of singleton births by gestational week, gender, and five-year time period (1978-1982, 1983-1987, 1988-1992, 1993-1997, 1998-2002) (Alexander, 1996). Term LBW was defined as ≥ 37 weeks gestation and birth weight <2500g.

Birth records for all of NYS (excluding NYC) were used to calculate expected number of births with each type of birth outcome. Using all singleton births during the 28-year study period (about 3.8 million births), statewide annual age-group rates for each outcome was calculated. Nine maternal age groups were used: 10-14, 15-17, 18-19, 20-24, 25-29, 30-34, 35-39, 40-44 and 45 and older. The annual expected number of births with the birth outcome is the annual statewide age-specific rate multiplied by the number of singleton births in the study area for that age group and year. The annual expected numbers are then summed across age groups and study years to get the total expected number. Observed and expected numbers for each birth outcome are presented. When the observed number is greater (or less) than the expected number, this is called an excess (or deficit). This process adjusts for differences due to the distribution of age and year of birth in the study area and the comparison population (NYS, excluding NYC). When the observed number of any birth outcome is fewer than six, results are not presented in order to protect confidentiality.

Several outcomes being studied, including LBW and pre-term birth, have been linked to lower socioeconomic status. The study area is different from the comparison area (NYS, excluding NYC) in measures of socioeconomic status, race, and ethnicity. Therefore, the analyses used information about the mother and the pregnancy to take some of these differences into account. We do not have any direct measure of socioeconomic status however. Logistic regression modeling was used to analyze the risk of each birth outcome with respect to the potential exposure. Mothers living inside the study area boundary are considered exposed. The following information from the birth certificate was included in the models as potential confounders: baby's gender and year of birth, mother's age (less than 19, 19-34, 35+ years), education (less than high school, high school to some college, 4+ years college), race (white, non-white), number of previous live births (0, 1, 2, 3+), and prenatal care. 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). For each outcome, we present the adjusted odds ratio (OR) and its 95 percent confidence interval (CI) for exposure status. An OR above (or below) 1.0 with a 95 percent CI that does not include 1.0 is considered a statistically significant excess (or deficit).

3.5 Birth defects

Records of birth defects for singleton births for 1983-2005 (23 years) were obtained from the NYS DOH Congenital Malformations Registry (CMR). Table 2 lists categories of birth defects that are most appropriate to evaluate for VOC-exposed populations, based on current research findings. In this review, all types of reportable birth defects were reviewed. 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, ICD-9 Codes 740-759.

By geocoding the mother's address from the birth defect records (see section 3.7), we identified specific infants born with birth defects during the 23-year period. The expected number of total birth defects reportable to the NYS CMR for the same timeframe for NYS (excluding NYC) was calculated and compared to the total number of birth defects observed. The pattern of types of birth defects was also reviewed to look for unusual patterns in the number and types of defects, with specific attention to the defects associated in the literature with VOC exposures. These defects include neural tube defects, cardiac defects, cleft lip and cleft palate, and choanal atresia (Table 2).

3.6 Cancer

Cancer reports for the years 1980-2005 (26 years) were obtained from the NYS DOH Cancer Registry. The Cancer Registry contains an electronic record for all cases of cancer diagnosed among NYS residents beginning in 1980. Cancer cases in the study area were identified by geocoding (mapping) the patient's address at diagnosis using Cancer Registry record address information (see section 3.7). NYS DOH evaluated the incidence of all cancers combined and the fol-

lowing specific cancer sites (National Cancer Institute, SEER site recodes, 2003): breast, females only (SEER site recode 26000); lung (22030); colorectal (21041-21052); esophagus (21010); stomach (21020); other digestive (21030 and 21060-21130); prostate, (28010), urinary system (29010-29040); blood-forming (33011-35043); and brain and other nervous system (31010 and 31040). Since the study area population was primarily white (98 percent), NYS cancer incidence rates for whites only were used for comparison.

Cancer incidence was evaluated for specific anatomical sites (e.g., breast, lung), some site groupings (e.g., blood forming, urinary system), and for all cancers combined. Although cancer includes many etiologically diverse diseases, we grouped specific cancer sites to some extent as a way to evaluate general patterns because of the relatively small number of cases. In addition, we evaluated cancer incidence for males, females, and males and females combined. When the observed number of cases is fewer than six, results are not presented in order to protect patient confidentiality.

Cancer incidence was evaluated by determining the number of observed and expected cases in the study area and computing standardized incidence ratios (SIR) and 95 percent confidence intervals (95 percent CI). To compute the expected number of cancer cases, the NYS Cancer Registry provided counts for all cancers combined and for specific cancer sites or site groupings for each year in the study period for whites only for all NYS (excluding NYC). The Cancer Registry also provided population counts for eight age groups (0-9, 10-19, 20-29, 30-44, 45-54, 55-64, 65-74, and 75+ years) for the NYS (excluding NYC) comparison population. For the Hopewell Precision study area, population estimates for the U.S. Census blocks comprising the study area were tabulated for the study years. Population counts from the 1980, 1990, and 2000 U.S. censuses were used to estimate the population for each of the years between census years. Because there was no information on population growth for the study years 2001-2005, the population for 2000 was used for these years. The annual expected number of cancer cases was computed by multiplying the NYS (excluding NYC) gender- and age-specific cancer incidence rates by the corresponding annual gender- and age-specific study area populations. The annual expected numbers are then summed across gender, age, and years to get the total expected number of cancer cases. This process adjusts for any differences in the distribution of age and gender and year of diagnosis in the study area and the comparison population (NYS, excluding NYC).

Gender- and age-adjusted SIRs were calculated by dividing the observed number of cancer cases by the expected number of cancer cases. The Poisson probability distribution (which is used to describe the occurrence of rare events) was used to calculate 95 percent CIs. An SIR greater than 1.0 (or SIR less than 1.0) with a 95 percent CI that does not include 1.0 is considered a statistically significant excess (or deficit).

3.7 Geocoding births, birth defects, and cancer cases

We obtained the residential address for all births, birth defects, and cancer cases within ZIP code 12533, which contains the entire study area. To capture records with incorrect ZIP codes or a missing ZIP code, we also obtained the addresses for all records in the neighboring ZIP code 12590 and in Dutchess County without a ZIP code. The addresses were put into the U.S. Postal Service standard format. Using commercially available geographic information system (GIS) software, the addresses were then 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 were then “captured” and classified as exposed. In order to protect confidentiality, no maps of individual case locations are reported.

4.0 RESULTS

4.1 Geocoding

Birth outcomes

A total of 19,516 birth records from ZIP codes 12533 (6,852 birth records) and 12590 (11,812 birth records) and Dutchess County births with no ZIP code (852) were selected for geocoding to determine if the mothers resided in the study area at the time of birth. Almost all (99.9 percent) 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 229 birth records being assigned to the exposed group (i.e., in the study area).

Cancer

The NYS Cancer Registry provided 5,659 cancer cases with residential addresses at the time of diagnosis in ZIP Codes 12533 and 12590 for 1976-2005. Only cases diagnosed during 1980-2005 were used in the analysis because these are the years for which computerized data are considered complete. Of these cases, 94 percent (5,325 records) were assigned geographic coordinates to the degree of accuracy necessary to determine if they were in the study area. Records that did not contain enough address information to be geocoded were investigated further, and none were determined to be in the study area. Ninety-three cancer cases were assigned to the exposed group (i.e., in the study area).

4.2 Low birth weight (LBW), prematurity, growth restriction, and sex ratio

Results are presented in Table 3. There were a total of 229 births among residents in the study area during 1978-2005. Ten 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, birth weight, or combination of gestational age and birth weight. Eight percent of births in NYS (excluding NYC) were excluded from the analysis for these same reasons. The exclusions resulted in 205 births in the Hopewell study area.

In the study area, fewer than six LBW births were observed and about 10 were expected (a deficit). Despite the large difference between the observed and expected numbers, the confidence intervals from the adjusted analyses include the value of one, indicating that the deficit of LBW, moderately LBW, and very LBW are not statistically significant. For premature births, the observed number of 14 is close to the expected number of 16. The numbers for the subsets of moderately and very preterm births (numbers not shown) are also very close to the expected values. There were eight SGA births in the study area compared to 19 expected, a statistically significant deficit. There is also a deficit of term LBW, but because the observed number is zero, no confidence interval can be calculated. The observed number of male births in the study area was 99 (male to female ratio 0.48) and the expected number was 105 (0.51), a small difference that was not statistically significant.

4.3 Birth defects

Eleven birth defects were detected in the study area over 23 years (1983-2005). This number is very close to the number expected, 10.1. (This slight difference is not statistically significant.) Because the study area and the number of birth defects are small, numbers are not provided for separate categories of birth defects. A variety of defects were represented in the total, with heart defects and defects of the renal pelvis and ureter reported most frequently. This is similar to the general pattern in NYS. None of the small number of observed heart defects are classified as major heart defects. There was also no evidence of an excess of the other types of defects associated with VOC exposures in other studies.

4.4 Cancer

Cancer analysis results are presented in Table 4. For males and females combined, the SIRs are shown for all cancer types, but observed and expected numbers are not shown when the number observed is less than six. For males and females separately, the observed and expected numbers and SIRs are not presented if the observed number for either males or females is less than six. The total number of observed cancer cases (89) in the study area is very similar to the expected number (92.7). For eight of the 11 cancer groupings evaluated, there is no evidence of a difference between the study area and NYS (excluding NYC). The SIR's for these eight categories of cancer (cancers of blood forming tissue, brain and other nervous system, colorectal, lung, other digestive, urinary system, prostate, and female breast) are between 0.8 and 1.3. For two types of cancer, the SIRs were more elevated (specifically, above 1.3) but not statistically significant: esophagus (SIR=3.3, 95 percent CI 0.7-9.7) and stomach (SIR=2.9, 95 percent CI 0.9-6.9). While the "other" grouping of cancers showed a relatively low SIR of 0.6, there were no statistically significant deficits.

The cancers of the esophagus were diagnosed among males and females at ages ranging from the late forties to early sixties, and all were diagnosed in the 1980s and early 1990s. The stomach cancers were also diagnosed in both males and females at ages ranging from late sixties to late eighties, and most of these cancers were diagnosed after 2000.

5.0 DISCUSSION

5.1 Interpretation

This health statistics review found no evidence of an excess of adverse birth outcomes in children born to residents of the Hopewell Precision study area compared to the State (excluding NYC) during 1978-2005 (LBW, prematurity, growth restriction, and sex ratio) or 1980-2005 (birth defects). There was a statistically significant deficit (fewer than expected) of small for gestational age births. There was no evidence of an excess of total birth defects or any elevation of major heart defects or the other defects associated with VOC exposures in other studies.

This review found no statistically significant excesses of total cancers or specific types of cancer diagnosed among residents of the Hopewell Precision study area compared to the State (excluding NYC) from 1980-2005. There was no evidence of an excess of lymphoma or kidney cancer, two types of cancer associated with VOC exposure in other studies (Wartenberg, 2000). Esophageal cancer, associated with VOC exposures in some studies (ATSDR 1997a, Hansen et al., 2001, Raaschou-Nielsen et al., 2003), was elevated in the study area, but the elevation was not statistically significant.

While no excesses of adverse birth outcomes or cancer were observed, this type of review does not allow conclusions to be made about whether any particular birth outcome or cancer diagnosis was or was not the result of a VOC exposure.

5.2 Limitations

In drawing conclusions from this health statistics review there are several limitations that need to be addressed. First, 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. It is expected that when conducting 20 different statistical tests, one result will turn out to be statistically significant on the basis of chance alone. The second limitation is the power of the statistical test, which is the chance that you will find a statistically significant elevation or deficit when, in fact, a true increase (or decrease) exists. Statistical power increases as the number of expected cases increases. For rare health outcomes, such as birth defects and cancers, it is unlikely that a small population will provide enough cases to detect elevations, even if they truly exist. For this study, there was 90 percent power of detecting a doubling in incidence, if it truly existed, only for preterm births, SGA births, and all cancers combined, which had expected

numbers of 16 or more. (An expected number of 12 or more provides 80 percent power, which is often used as the cut-off for adequate statistical power.)

Another limitation related to those discussed above 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 number 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.

A health statistics review cannot take into account personal information that may be related to the health outcomes, such as medical history, dietary and lifestyle choices (e.g., smoking and drinking), and occupational exposures to other chemicals. In addition, exposure misclassification is a limitation of this type of review and can occur because of incomplete knowledge about actual exposure and migration in and out of the study area. Although drinking water and soil vapor sampling was conducted in the Hopewell Precision Contamination site, there is no way to know if individuals in the study area were exposed or to what extent (including the duration of the exposure, the amount of time residents spent in the home each day) and if there were other exposure pathways (e.g., occupational). 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 could not be 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. For cancers, the review was limited to cases diagnosed when the patient was living in the study area. Most cancers begin to develop long before they are diagnosed (called latency) and this review could not take into account whether or for how long the patient lived in the study area before being diagnosed with cancer. People who had lived in the study area but moved away before being diagnosed, were not included.

6.0 CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

This review found that the numbers of adverse birth outcomes diagnosed in children born to residents of the Hopewell Precision study area were either lower or similar to the number expected. The pattern of specific types of birth defects did not appear unusual. The review of cancer showed no statistically significant elevations. Conclusions from this review are limited due to the small population in the exposed area and the small numbers of outcomes. In addition, cancer and birth outcomes were the only types of health outcomes for which data were available for inclusion in this type of review.

6.2 Recommendations

NYS DOH and ATSDR make the following recommendations:

1. Include the Hopewell Precision study area in the combined health statistics review currently being conducted for several other smaller sites in NYS with similar VOC exposures. The larger combined review may be able to draw stronger conclusions than this review because there will be a larger population and larger expected numbers of birth outcomes, birth defects, and cancers.
2. Work with area residents to address additional health concerns that could not be included in this review. This effort includes learning more from the community about their additional health concerns and addressing such concerns by developing a follow-up plan jointly with interested residents. This process may involve working with other agencies, consulting additional experts, and further study, if feasible.

7.0 GLOSSARY

Age adjustment: Age adjustment: A statistical method that attempts to take into account the differing age distribution of the group being studied and the comparison population.

Confidence interval (95 percent CI): The range around an estimate (such as an odds ratio or standardized incidence ratio) that conveys how precise it is. If the same study was repeated, 95 out of 100 times the result would be within the lower and upper values of the confidence interval. The width of the confidence interval depends on the precision of the estimate and tends to be wider in studies with a smaller number of observations.

Confounding: Confounding occurs when a measure of the association between an exposure and an outcome (e.g., odds ratio) is affected by another factor, a confounder or confounding variable, that is associated with both the exposure and the outcome. An adjusted analysis attempts to take the confounder into account.

Odds ratio (OR): A measure of association that quantifies the association between an exposure and a health outcome. An odds ratio greater than 1.0 means that the exposed group is more likely to have the outcome; An odds ratio less than 1.0 means that the exposed group is less likely to have the outcome.

Standardized incidence ratio (SIR): The number of an outcome that is observed in a group being studied divided by the number that is expected if the rate of occurrence of the outcome were the same as a comparison population.

Statistical significance: A measure of how likely it is that an association (such as an odds ratio or standardized incidence ratio) could have occurred by chance alone. When 95 percent confidence intervals are used with an odds ratio or standardized incidence ratio, a statistically significant association is when the confidence interval does not include 1.0.

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PREPARERS OF THE REPORT

New York State Department of Health Authors

Elizabeth Lewis-Michl, Marta Gomez, Karen Nolan, Kamal Nain-Siag,
June Beckman-Moore, James Bowers
Research Scientists
Bureau of Environmental and Occupational Epidemiology

Don Miles
ATSDR Grant Principal Investigator
Bureau of Environmental Exposure Investigation

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Agency for Toxic Substances and Disease Registry

Mohammed Uddin, Medical and Technical Project Officer
Health Investigations Branch, Division of Health Studies

Gregory V. Ulirsch, Technical Project Officer,
Division of Health Assessment and Consultation

Figure 1. Map of the Hopewell Precision study area, Hamlet of Hopewell Junction, Dutchess County, New York

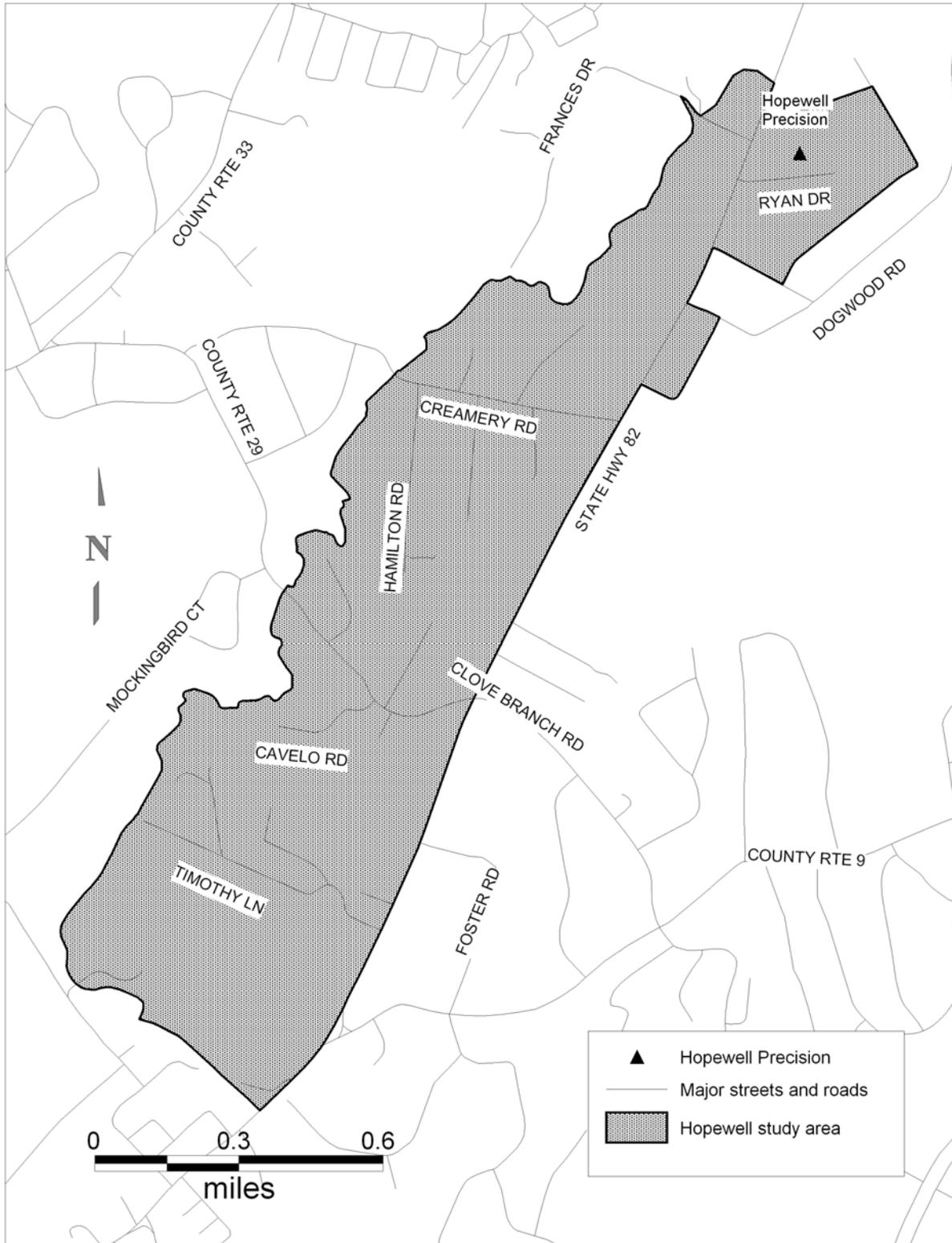


Table 1. Demographics of the Hopewell Precision Contamination Site Health Statistics Review Study Area: Hamlet of Hopewell Junction, Town of East Fishkill, Dutchess County, New York; and New York State, excluding New York City: 1980, 1990, and 2000

Demographics	Hopewell Precision study area			New York State, excluding NYC		
	1980^{1,2}	1990^{3,4}	2000^{5,6}	1980^{1,2}	1990^{3,4}	2000^{5,6}
Total Population	701	722	858	10,486,433	10,667,891	10,968,179
Males	52%	49%	48%	48%	49%	49%
Age (years)						
<6	8%	8%	7%	8%	8%	8%
6-19	28%	20%	23%	24%	19%	20%
20-64	54%	60%	58%	57%	59%	58%
>64	10%	12%	12%	12%	13%	14%
Race and ethnicity						
White	98%	98%	98%	92%	90%	85%
Black	2%	1%	<1%	6%	7%	8%
Native American	0%	0%	<1%	<1%	<1%	<1%
Asian	<1%	<1%	<1%	1%	2%	2%
Pacific Islander	0%	--	0%	<1%	<1%	<1%
Other	0%	<1%	<1%	1%	1%	2%
Multi-Racial	--	--	1%	--	--	2%
Percent Minority*	3%	3%	7%	9%	13%	18%
Percent Hispanic	1%	1%	6%	2%	7%	6%
Income						
Median household income	\$23,107	\$60,897	\$74,712	\$18,889	\$35,711	\$47,517
% below poverty level	5%	3%	<1%	9%	9%	10%

* Percent minority includes the non-white categories.

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Table 2. Birth Defects Groupings Evaluated in the Hopewell Precision Contamination Site Health Statistics Review Study Area

Birth Defect Group	ICD-9 code	Description
Total Reportable Defects	--	All major structural defects, chromosomal anomalies and metabolic syndromes reportable to the CMR*
Structural Defects	740-759	All major structural defects
Neural Tube Defects	740.X 741.X 742.0X	Anencephalus Spina bifida Encephalocele
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
Major Cardiac Defects	745.0 745.1 745.2 746.0 746.1 746.3 746.4 746.7 747.1 747.3	Common truncus Transposition of great vessels Tetralogy of Fallot Anomalies of pulmonary valve Tricuspid atresia and stenosis Congenital stenosis of aortic arch Congenital insufficiency of aortic valve Hypoplastic left heart syndrome Coarctation of aorta Anomalies of pulmonary artery
Cleft lip/cleft palate	749.00-749.04 749.10-749.14 749.20-749.25	Cleft palate Cleft lip Cleft palate with cleft lip
Choanal atresia	748.00	Choanal atresia

Abbreviations: X = 0 through 9

* See the NYS DOH Congenital Malformation Registry Handbook for a complete listing of reportable birth defects and conditions (NYS DOH, 2004).

Table 3. Comparison of Observed versus Expected Numbers of Birth Outcomes (Low Birth Weight, Prematurity, Growth Restriction, Sex Ratio), Hopewell Precision Contamination Site Health Statistics Review Study Area: 1978-2005

Birth outcomes	Number of births with the outcome, study area		Adjusted analysis**		
	Observed*	Expected	OR	95% CI	
				Lower	Upper
Low birth weight (<2500 g)	<6	9.9		0.11	1.06
Moderately low birth weight (1500-2500 g)	<6	8.2		0.07	1.09
Very low birth weight (<1500 g)	<6	1.7		0.10	4.96
Preterm birth (<37 weeks)	14	15.9	0.91	0.52	1.61
Moderately preterm (32-37 weeks)	<6	13.9		0.48	1.62
Very preterm (<32 weeks)	<6	2.1		0.29	4.66
Small for gestational age	8	18.6	0.41	0.19	0.88
Term low birth weight	0	3.9	†		
Sex ratio					
Number of males	99	105.1			
Males/females	0.48	0.51	0.91	0.68	1.21

Abbreviations: 95% CI = 95% Confidence Interval; SIR = Standardized Incidence Ratio; OR = Odds Ratio.

* Observed numbers less than six and ORs based on these numbers are not presented to protect the confidentiality of the subjects.

** Logistic regression adjusted for year of birth, mother's age (<19, 19-34, 35+ years), sex of baby, education (<high school, high school-some college, 4+ years college), race (white, other), total previous live births (0, 1, 2, 3+), and prenatal care (adequate, intermediate, inadequate).

† Exact estimates could not be computed (OR<0.001, 95% CI <0.001,>999).

Table 4. Comparison of Observed versus Expected Numbers of Incident Cancer Cases, Hopewell Precision Contamination Site Health Statistics Review Study Area: 1980-2005

Type of Cancer	Males					Females					Males and Females				
	# cases		SIR	95% C.I.		# cases		SIR	95% CI		# cases		SIR	95% CI	
	Obs.	Exp.		Lower	Upper	Obs.	Exp.		Lower	Upper	Obs.	Exp.		Lower	Upper
Blood forming	--	--	--	--	--	--	--	--	--	--	6	7.9	0.8	0.3	1.6
Brain/other nervous system	--	--	--	--	--	--	--	--	--	--	--	--	1.3	0.2	4.8
Colorectal	6	6	1.0	0.4	2.2	7	5.8	1.2	0.5	2.5	13	11.8	1.1	0.6	1.9
Lung	--	--	--	--	--	--	--	--	--	--	13	14.1	0.9	0.5	1.6
Esophagus	--	--	--	--	--	--	--	--	--	--	--	--	3.3	0.7	9.7
Stomach	--	--	--	--	--	--	--	--	--	--	--	--	2.9	0.9	6.9
Other digestive**	--	--	--	--	--	--	--	--	--	--	--	--	1.1	0.4	2.7
Urinary system	--	--	--	--	--	--	--	--	--	--	6	7.5	0.8	0.3	1.7
Prostate	11	11	1.0	0.5	1.8						11	11	1.0	0.5	1.8
Female breast						15	14.1	1.1	0.6	1.7	15	14.1	1.1	0.6	1.7
Other†	--	--	--	--	--	--	--	--	--	--	10	17.8	0.6	0.3	1.03
TOTAL	46	46.1	1	0.7	1.3	43	46.6	0.9	0.7	1.2	89	92.7	0.95	0.8	1.2

Abbreviations: Obs.=observed, Exp.=expected, CI=confidence interval, SIR=standardized incidence ratio.

-- Observed numbers less than six and some SIRs based on these numbers are not presented to protect the confidentiality of the subjects.

** Includes anorectum, liver, other biliary, and pancreas.

† Includes melanoma, cancer of the cervix uteri, corpus uteri, uterus (not otherwise specified), testis, eye and orbit, other endocrine cancers, and miscellaneous cancers.