State of New Hampshire
Department of Health and Human Services
Division of Public Health Services

Pediatric Seacoast Cancer Cluster Investigation

A Summary of Investigation Findings as of April 30, 2017

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Executive Summary

Purpose: The Seacoast Cancer Cluster Investigation questionnaire was developed by the New Hampshire Department of Health and Human Services (NH DHHS) with input from multiple stakeholders in order to gather information on characteristics and potential exposures among those who were diagnosed with rhabdomyosarcoma (RMS) or pleuropulmonary blastoma (PPB). Development of the questionnaire was based on community concerns and the limited scientific literature investigating causes of RMS and PPB; the questionnaire was developed to be broad and inclusive.

Case Finding: A case definition was created to allow NH DHHS to investigate cases meeting common criteria. A case was defined as a person with laboratory-confirmed RMS or PPB diagnosed since 2001 in a person younger than 20 years old who spent at least 28 days (cumulative, in utero or after birth) in any of the following ten New Hampshire towns (10-town seacoast area): Greenland, Hampton, Hampton Falls, New Castle, Newington, North Hampton, Portsmouth, Rye, Seabrook, or Stratham at least six months prior to diagnosis.

A total of 40 individuals diagnosed with RMS or PPB were notified of the investigation and invited to participate if they self-identified as also meeting the geographic exposure criteria (unlike cancer diagnosis criteria, geographic exposure could not be evaluated through cancer registry data). Twenty-six questionnaires were mailed and hand delivered to individuals identified through the NH Cancer Registry and to former NH residents who reached out to DHHS about participation; 14 letters were mailed to individuals York and Essex counties, identified through the ME and MA cancer registries. A total of 7 questionnaires were returned to NH DHHS with informed consent for individuals meeting the case definition.

Results: The questionnaire evaluated a variety of factors including geographic exposures including residential air quality and water source and quality; prenatal history and exposures; medical history of cases and their family; and occupational and hobby related exposures for cases and their parents. The following is a summary of results.

Demographic Data and Cancer Diagnosis:

- Individuals diagnosed with RMS/PPB included in this investigation were diagnosed over the course of seven years (between 2004 and 2011); diagnoses did not cluster within any specific year.
- Four cases were female (57%), three were male (43%); the average age of diagnosis was five.

Geographic Exposures:

- Two of the seven respondents reported residence in the 10-town seacoast area prior to diagnosis; the remaining five reported visiting the 10-town area prior to diagnosis. Individuals reported spending time in most of the Seacoast towns. The majority of respondents reported spending time in Portsmouth (n=6), but no specific site in the city was noted. No other town was identified by a majority of respondents. There was no single consistent toxic site reported in close proximity to the majority of respondents.
- There were no common childcare facilities or schools reported. Two of the respondents reported attending a total of four different schools within the 10-town area.
- There were no patterns identified in data related to drinking water source or quality. Two of the seven respondents reported regularly consuming water from a public drinking water supply in the 10-town seacoast area; all others reported either public (n=4) or private (n=2) sources outside of the 10-town area, with one reporting both.

- Three respondents with a residence outside of the 10-town seacoast area reported that home air tests indicated elevated levels of radon. Radon exposure has not been linked to RMS or PPB in scientific studies.

Prenatal History:

- Aside from common use of prenatal vitamins, only two of the seven mothers reported use of any prescription medications during pregnancy. There were no common prescription medications taken and the medications reported are not known to be associated with RMS/PPB.
- There were no exposures reported for illicit drugs or tobacco prenatally.
- There were no reported exposures to x-rays or other medical radiologic scans or nuclear studies during pregnancy.

Individual Case and Family Medical History:

- No common prescription medications or childhood illnesses were identified in the majority of cases. The majority of individuals with RMS/PPB reported no childhood illnesses prior to diagnosis, and of the individuals who reported illness, most involved common childhood ailments such as allergies, asthma, or colds.
- There was no reported tobacco or illicit drug use among cases. One respondent reported case exposure to second-hand tobacco smoke.
- Exposure to medical x-rays was reported for two cases, and one additional case reported probable exposure to dental x-rays. No other radiological scans were reported and no exposure to radiation therapy was reported.
- Four out of seven respondents reported a family history of cancer; none of the cases were among immediate (1st degree) family members.
- There were no common genetic syndromes reported amongst respondents.

Occupational History and Hobbies:

- No parental occupations were reported that suggested chemical exposures to parents.
- No hobbies were reported for parents or cases that suggested chemical exposures.

Based on the responses, there do not appear to be any notable patterns to suggest a common exposure or etiology for the development of RMS or PPB among cases, and the findings do not support moving to a case-control study. Additionally, the scientific literature does not point to chemical or environmental exposures as a cause of RMS/PPB, and the majority of cases are thought to either occur sporadically, or to be associated with genetic family cancer syndromes.

The NH DHHS re-evaluated the number of RMS and PPB cases in the seacoast area in February of 2017 (one-year after the original report), and there have been no new cases of RMS/PPB identified in the 10-town seacoast area. We will continue to review and evaluate RMS and PPB cases reported to the NH State Cancer Registry as new data becomes available, and will reassess the need for ongoing monitoring over time. Even though our investigation has not shown a common identified exposure among RMS and PPB cases, further work is currently being performed in the Seacoast community to address concerns about potential exposure to environmental contaminants out of interest in protecting public health, and NH DHHS will continue to work closely with partners to help address these concerns.

Cancer Clusters

Background

According to the CDC, "a cancer cluster is defined as a greater than expected number of cancer cases that occurs within a group of people in a geographic area over a defined period of time". The CDC breaks this definition down further to describe "a greater than expected number" to mean an observed number of cases that is "greater than one would typically observe in a similar setting." To be considered a cluster, all cases need to be of the same type of cancer, or be types of cancer that have been scientifically linked to the same cause or exposure.[i]

Challenges and History of Efforts

There are limitations when a reported cancer cluster includes a small number of cases; a lack of statistical power may make it challenging to detect an association. Even in the situation when a greater than expected number of cancer cases is identified (i.e. a cluster is identified), it is challenging to identify whether there is a cause or common exposure. According to the National Cancer Institute at the National Institutes of Health, "a cancer cluster could be the result of chance" due to the random development of cases across an area and population and not have any identifiable cause.[ii] For this reason, cancer cluster investigations usually focus on identifying known causes of a cancer in an area with the purpose of eliminating exposures.

In a systematic review of over 400 cancer cluster investigations conducted throughout the nation, only one investigation yielded conclusive results, identifying an associated cause with certainty. Two additional investigations reported less certain associations between the cancers of concern and specific environmental exposures.[iii] Despite the rarity of conclusive findings about specific environmental associations in identified clusters, investigations continue to be an important function of public health departments and agencies. Even when a common cause cannot be identified, investigations present the opportunity for public education about cancer and prevention. Often times community engagement may lead to identification of local environmental concerns to be addressed.

Department of Health and Human Services Response

In March 2014, residents of Rye, NH, contacted the New Hampshire Department of Health and Human Services (DHHS) to report a possible cluster of rhabdomyosarcoma (RMS) cases among children in Rye. To determine whether the report was consistent with a cluster, DHHS followed Centers for Disease Control and Prevention (CDC) guidance, and used data from the New Hampshire State Cancer Registry to calculate the standardized incidence ratio (SIR) for adult and pediatric cancers (all cancer types) and adult and pediatric rhabdomyosarcoma among residents living in a five-town area including and surrounding Rye, NH.[iv,v] The SIR is a statistical calculation used to tell whether there is a greater than expected number of a cancer cases in an area based on a comparison population. More details about the calculations and findings can be found in the DHHS February 2016 report (http://www.dhhs.nh.gov/dphs/hsdm/cancer/documents/rhabdomyosarcoma2016.pdf). In summary, adult or pediatric cancers (all types) were not found in greater than expected numbers; however, the specific cancers of pediatric RMS and pediatric pleuropulmonary blastoma (PPB) were. The actual number of identified cases of these cancers, however, were small (< 5 cases for each type over a 10 year time period), which limited the ability to draw conclusions. The scientific literature was also reviewed to determine if there were any environmental or lifestyle factors known to be causative for these cancers. Additionally, the science was limited without any significant or consistent evidence for causes other than

genetic factors. The 2016 DHHS report concluded that a more detailed epidemiologic investigation would be unlikely to result in the identification of an environmental exposure to explain the greater than expected number of RMS and PPB.[v] Following the release of the report, a number of community members contacted DHHS indicating potential connections to the seacoast area with children diagnosed with RMS or PPB. Additionally, in the community meeting held following the release of the report, meeting participants identified additional potential environmental exposures in the area. Following these developments, DHHS decided that a systematic case investigation should be conducted to evaluate if there was a potential connection between cases of pediatric RMS and PPB and a common exposure.

According to data from the National Program of Cancer Registries (NPCR) and Surveillance, Epidemiology, and End Results (SEER) state registries, in 2013, the rate of RMS in children ages 0-19 in the United States was 0.466 cases per 100,000 children. RMS has been associated with various inherited or familial cancer syndromes, such as Li-Fraumeni syndrome and neurofibromatosis-1.[vi, vii, viii, ix] The World Health Organization classifies RMS into embryonal, spindle cell sclerosing, alveolar, and pleomorphic subtypes. About 80% of RMS is embryonal; 15-20% of RMS is alveolar. While there are some histologic similarities between RMS and PPB, especially in the early stages of the cancers, and some identified common genetic predispositions, these are considered separate cancers. Studies reported in the scientific literature have not identified environmental exposures as a risk factor for RMS or PPB.

Given public concern over the identified clusters, DHHS conducted a case investigation (case series) through distribution of a questionnaire to obtain more information from families affected by RMS or PPB to in order to describe patient characteristics including environmental exposures; demographics; and clinical, family and social histories in order to identify potential common exposures. It is important to note that a limitation to case series investigations is that they are descriptive and performed primarily to identify patterns and generate hypotheses, not to prove cause-and-effect.

Stakeholder Involvement and Response

NH DHHS involved a variety of stakeholders in the pediatric RMS and PPB cancer cluster investigation, including state agencies (Department of Environmental Services), local health officials, community members, elected officials, federal agencies (United States Centers for Disease Control and Prevention and the Environmental Protection Agency), and academics.

In addition to following guidance established by national public health agencies and experts, NH DHHS convened a Community Advisory Group (CAG), comprised of members of the local community and elected representatives, which was tasked with reviewing and informing investigation activities.

In response to the Seacoast Cancer Cluster investigation, The Governor's Task Force was also established by former Governor Maggie Hassan in June of 2016 to bring together local, state, and federal stakeholders affected by the cancer cluster investigation on the Seacoast to coordinate and maintain consistent communication and strategy to address community concerns. The Task Force also developed subcommittees to focus on specific areas of environmental concerns in the seacoast area that were raised by community members. The work of the Task Force's subcommittees is separate from the DHHS cancer cluster investigation. Further detail about the Governor's Taskforce can be accessed online at http://www.dhhs.nh.gov/dphs/gtfscc/index.htm.

Case Questionnaire Investigation Methods

As part of the investigation, DHHS developed a questionnaire to gather information on characteristics and potential exposures from those who were diagnosed with RMS or PPB. The questionnaire is comprehensive and was developed based on community concerns and the limited scientific literature investigating causes of RMS and PPB. It was reviewed by the stakeholder groups noted above, including the CDC, RMS researchers, and the CAG, and it was modified based on feedback.

The investigation was submitted to Institutional Review Boards in all participating states (New Hampshire, Maine, and Massachusetts). The complete protocol and case questionnaire can be found here (http://www.dhhs.nh.gov/dphs/hsdm/cancer/rms-investigation.htm).

Objectives

The stated objectives of conducting the RMS/PPB investigation were as follows:

1. To determine if a potential common exposure could be identified among cases studied.
2. To inform DHHS' decisions on next steps for further investigation or monitoring.

Case Definition

A case definition was created to allow DHHS to investigate cases meeting common criteria. A case was defined as a person with laboratory-confirmed RMS or PPB diagnosed since 2001 in a person younger than 20 years old who spent at least 28 days (cumulative, in utero or after birth) in one of the following ten New Hampshire towns: Greenland, Hampton, Hampton Falls, New Castle, Newington, North Hampton, Portsmouth, Rye, Seabrook, or Stratham at least six months prior to diagnosis.

The February 2016 DHHS Report focused on the five-town area (Rye, New Castle, Portsmouth, North Hampton and Greenland). However, because of public concerns about environmental exposures in other areas of the Seacoast (e.g. the Seabrook Nuclear Power Plant), the evaluated geographic area was expanded to the ten-town area noted above to ask individuals about environmental exposures in those areas.

Twenty-eight days of cumulative time spent in the ten-town area was a number chosen as a conservative approach to assess for potential environmental exposure in these areas. In developing the case definition and protocol, scientific and public health experts were consulted, and the consensus was that a period of time longer than 28 days was standard for use as criteria in cancer studies; therefore, the selection of 28 days should not be interpreted as a worrisome amount of time to have been in the area but rather as an attempt to include additional cases and understand potential common exposures in the ten-town seacoast area.

Case Finding

New Hampshire

The New Hampshire Cancer Registry was used to generate a list of individuals diagnosed with RMS or PPB who were under 20 years of age at the time of diagnosis, and who were diagnosed with RMS or PPB after 2001. The parents or guardians of these individuals were notified of our investigation through a letter from DHHS sent on October 11, 2016. They were provided with the Case Definition to evaluate whether their child met the inclusion criteria for the investigation. They were also provided with an Informed Consent Form and the Questionnaire, which they were asked to return if their child met the case definition and they wished to participate. Participants were provided with a contact number and

email address to use for questions, and were offered the option of taking the questionnaire via telephone. Reminder letters to encourage participation were mailed out to those who did not respond to the initial request on January 3, 2017. A total of 26 questionnaires were mailed and hand delivered to individuals identified through the NH Cancer Registry and to former NH residents who reached out to DHHS about participation. It is important to note that while we were able to use registry data to determine whether or not individuals met the diagnosis criteria of the definition, we were not able to evaluate whether or not individuals met the geographic exposure criteria; as such, it was not expected that all 26 recipients would be eligible to participate.

Neighboring States

To reach individuals diagnosed with RMS or PPB from neighboring states who might have visited the seacoast area, NH DHHS coordinated with staff from the Maine and Massachusetts Department of Health. Staff from each of the respective state cancer registries generated a list of individuals residing in counties contiguous to the seacoast area (York County in Maine and Essex County in Massachusetts) who met the age and diagnosis criteria of the case definition. Again, geographic exposure could not be evaluated. Letters were sent with details about the investigation and the full case definition, with an invitation to contact NH DHHS to participate. A total of 14 letters were mailed to individuals identified through the ME and MA cancer registries.

Data Collection and Analysis

Participation in the investigation was voluntary, and it was not expected that all who received a questionnaire or letter would meet the case definition for spending time in the seacoast area. As of April 30th, a total of seven completed questionnaires for individuals meeting the case definition were returned with informed consent.

The data from completed questionnaires was entered into a spreadsheet stored on a secure server. Paper copies of the questionnaires were stored in a locked file cabinet at DHHS. Descriptive analysis was conducted by DHHS staff.

To protect the privacy and confidentiality of individuals and families, personally identifiable information from questionnaire responses is not publicly reported in accordance with NH DHHS policy. For this reason this report summarizes responses and does not provide specific information that may be personally identifying, including names, addresses, and occupations.

Results

The following sections include a description of data collected and a summary of findings from the returned case questionnaires with informed consent as of March 31, 2017.

Summary of Demographic and Cancer Diagnosis Information

A total of 7 questionnaires were returned; 5 for cases with a confirmed diagnosis of RMS/PPB through the cancer registry, 2 for probable cases of RMS/PPB (reported by respondents who reached out to NH DHHS to participate, but not confirmed through the registry or by pathology laboratory report). Four (57%) were female, three (43%) were male. The average age of diagnosis was five years, and all cases were diagnosed at younger than 10 years of age. All cases were diagnosed between 2004 and 2011. Two of the cases reported residence in the 10-town area prior to diagnosis, 5 of the cases reported visiting the 10-town area prior to diagnosis for various reasons including errands, extra-curricular activities, and visiting family and friends.

Geographic Exposures

The questionnaire asked about geographic and environmental exposures in the 10-town area of Greenland, Hampton, Hampton Falls, New Castle, Newington, North Hampton, Portsmouth, Rye, Seabrook, and Stratham.

Residential and Other Exposure to the 10-town Area

Two out of the seven respondents reported childhood residence in the 10-town area. Both children attended preschool and school in the town, but they did not attend the same schools. The remaining five cases reported living in surrounding towns outside of the 10-town area, with travel into the 10 towns culminating in at least 28 cumulative days spent in area at least 6 months or more prior to diagnosis (see case definition). No respondents reported attending childcare within the 10-town area. The majority of respondents reported spending time in Portsmouth (n=6), but no specific site in the city was noted. No other town was identified by a majority of respondents.

Residential Water and Air Quality

There were no notable patterns identified in data related to drinking water source or water quality. Respondents for two RMS/PPB cases reported water from the same public drinking water source within the 10-town area, with years of residence overlapping. Of the remaining five cases all reported drinking water sources from outside the 10-town area: one reported use of a private well, three reported three different public drinking water sources and one reported both. No single public water system was consistently identified and there were a total of five different public drinking water systems reported.

One respondent (with a residence outside of the 10 town area) reported that a home drinking water test indicated elevated levels of radon and iron. Review of the literature has not linked radon or iron exposure to RMS or PPB.

Three respondents reported that air tests indicated elevated levels of radon (all with a residence outside of the 10-town area); of these three cases, one reported mitigation. Again, radon exposure has not been linked to RMS or PPB.

Self-Reported Proximity to Toxic Sites

Respondents were asked to report known proximity to toxic sites (within 10 miles). A distance of 10 miles was chosen to be inclusive, there is not an expectation that contaminants would travel such a distance. A total of two cases reported proximity to toxic locations within the 10-town area. Sites reported within the 10-town area included: Coakley Landfill, Pease Tradeport, Schiller Station, and Seabrook Station. Additional toxic sites reported within close proximity to respondents, but outside of the 10-town area include: the Portsmouth Naval Shipyard, a Barrington superfund site (unspecified), the Collins & Aikman site, the Rochester landfill, the Saco Municipal landfill, the Saco Tannery Waste Pits, and an unspecified landfill. The Portsmouth Naval Shipyard was reported by two respondents, all other sites outside of the 10-town area were each reported by one respondent. Detail about known sites is accessible through the Department of Environmental Services at http://www.des.nh.gov/onestop/index.htm.

Table 8. Number of cases reporting proximity (within 10 miles) to toxic location within 10-town area

Town/City	# of cases with prenatal or childhood residence
Coakley Landfill	1
Pease Tradeport	2
Schiller Station	1
Seabrook Station	1

Prenatal History

The questionnaire asked about prenatal history, including detail about residence, water source(s), prenatal exposures, and general information about pregnancy and birth outcomes. Questions specific to prenatal exposures and birth outcomes were asked based on limited scientific literature showing possible associations between RMS and:

- Late or no prenatal care[x]
- Parental age at birth[xi, x]
- Infant birth size and weight [xii, xiii]
- Abnormal vaginal bleeding during pregnancy[xiii]
- Parent use of tobacco or illicit drugs[xi, xiv]
- Prenatal X-ray exposure[xv]
- Prescription drug use pre/perinatally[xi, xvi, xvii]

The reported maternal age at birth ranged from 26 to 40 years (mean= 32 years of age), with one respondent not reporting maternal age. The reported paternal age at birth ranged from 28 years to 37 years (mean= 32 years of age). Four out of the six mothers for whom age was reported were over the age of 30 at the time of birth. The average gestational age at birth for RMS/PPB cases was 39 weeks (range from 35 weeks to 40 weeks). Two cases were born preterm, which is defined by the American Congress of Obstetricians and Gynecologists as birth before 37 weeks of gestation. One of the cases was of low birth weight.

Table 1. Gestational age and birth weight of cases

Gestational Term Classification*/Birth Weight Classification**	# of Cases
preterm/low birth weight	1
preterm/ normal birth weight	1
full term/ normal birth weight	5

*Term classifications are based on definitions from the American Congress of Obstetricians and Gynecologists

**Birth weight classifications are based on categories adopted by the United States Department of Health and Human Services, Health Resources and Services Administration

Five out of seven mothers reported taking prenatal vitamins during their pregnancy (Table 2); prenatal vitamins were not noted to be of concern in the literature about RMS/PPB. Two out of seven cases reported taking prescription medications during pregnancy, but of those mothers reporting taking prescription medications, there were no common medications taken and medications reported are not known to be associated with an increased risk.

Table 2. Medications taken by birth mother during pregnancy by case

Medication Class	# of Cases
Insulin	1
Levothyroxine	1
Vitamins (prenatal)	5

As show in Table 3, all RMS/PPB case respondents reported that there was no prenatal exposure to tobacco (by birth-mother or anyone else in the birth-mother's home) and no prenatal exposure to recreational drug use. There was no reported exposure to x-rays or other medical radiologic scans or nuclear medicine studies during pregnancy.

Table 3. Prenatal exposures for cases

Exposure type	# of Cases
Tobacco (use by mother)	0
Tobacco (second-hand exposure through others in the home during pregnancy)	0
Recreational drug use	0
X-rays, radiologic scans, nuclear studies	0

None of the respondents reported anemia during pregnancy. One respondent reported vaginal bleeding during pregnancy, and one reported decreased fetal movement.

Medical History

Case Medical History

The questionnaire also asked about individual medical history for the person diagnosed with RMS/PPB, including information about illnesses and medications taken prior to diagnosis, genetic test results, and health related exposures.

No common prescription medications or childhood illnesses were identified in the majority of cases. Four cases had no reported childhood illness prior to diagnosis. Illnesses reported among the remaining three cases included allergy induced asthma, seasonal allergies, colds, flu, abscessed tooth, and scoliosis. In addition to reporting illnesses, respondents reported medication use prior to diagnosis, which is shown in Table 4.

Table 4. Medications taken by cases

Medication Class	# of Cases
Antihistamines (oral)	2
Antipyretics/analgesics*	2
Bronchodilators	2
Fluoride	1
Proton pump inhibitors	1
Steroid (inhaled or topical)	2
Vitamins	1
Other**	1

*Includes acetaminophen, nonsteroidal anti-inflammatory drugs

**Reported as "cold medicine"

Related to other exposures, there was no reported tobacco use or recreational drug use among individuals diagnosed with RMS/PPB. One respondent reported case exposure to tobacco smoke from someone who spent time with the child before diagnosis. There was reported exposure to medical x-rays for 2 cases (head/skull and chest imaging), and probable exposure reported for dental x-rays for 1 additional case. The known medical x-ray exposures preceded diagnosis of RMS/PPB by at least two years in both cases. There was no exposure reported for other radiological scans or nuclear medicine studies. No exposure to radiation therapy was reported.

There were no common genetic syndromes reported among the majority of respondents.

Table 5. Child exposures experienced directly by cases

Exposure type	# of Cases
Tobacco (use by case)	0
Tobacco (second-hand exposure)	1
Recreational drug use	0
X-rays (including reported confirmed/probable exposure)	3
Other radiologic scans or nuclear studies	0
Radiation therapy	0

Family Medical History

The questionnaire asked about family medical history, including data about cancer diagnoses and genetic test results.

Four out of seven respondents reported a family history of cancer. None of the reported cases were among immediate (1st degree) family members. There were no genetic syndromes reported among family members of cases.

Table 6. Types of cancer reported among family members of cases

Reported Cancer Type	# of Cases
Breast cancer	2
Prostate cancer	1
Melanoma	2
Thyroid cancer	1
Other tumor type	1

Occupational and Hobby Related Exposures

The questionnaire asked about hobbies and occupations in those diagnosed with RMS/PPB and their parents/guardians. This was asked as limited scientific literature has evaluated for associations between occupational exposures and RMS[xviii, xix]

Occupational History and Hobbies of Parents

There was no duplication of occupation or occupational hazards reported among parents of cases. Parental occupational exposure to radiation was reported for one case, prior to and after the child's birth. Similarly, there was no noted duplication of hobbies or exposure to chemicals through hobbies across cases. One parent reported exposure to lawn care chemicals.

Child's Hobbies

There were no hobby related chemical exposures reported. Reported hobbies included playing with friends, participating in sports (including soccer, gymnastics, and swimming), painting, playing with toys, watching television; and visiting parks and beaches.

Conclusion

The case questionnaire was designed to be broad and inclusive, and was developed based on the few published scientific studies evaluating for associations with RMS/PPB, along with expert and community input. It was designed to be comprehensive, and to capture data about potential exposures or commonalities across cases, with the goal of providing data to evaluate for possible trends. Based on the responses outlined in this report, there does not appear to be any notable patterns to suggest a common exposure or etiology for development of RMS/PPB.

In summary, individuals diagnosed with RMS/PPB included in this investigation were diagnosed over the course of seven years. Diagnoses did not cluster within any specific year. Only two individuals reported residence within the 10-town seacoast area (both attending different preschools and schools), and the others reported living in surrounding towns but visiting the seacoast area. Individuals reported spending time in most of the Seacoast towns. The majority of respondents reported spending time in Portsmouth (n=6), but no specific site in the city was noted. No other town was identified by a majority of respondents. There was no single consistent toxic site reported in close proximity to the majority of respondents.

There has been concern in the community around potential contamination of drinking water supplies from nearby environmentally contaminated sites; however, our investigation has not pointed to any specific drinking water source as a potential factor in the development of RMS/PPB in the seacoast area. Out of the seven respondents, there were five different public drinking water systems and one private drinking water well that were identified as residential sources of drinking water; only two of the individuals reported regularly consuming water from public drinking water supplies in the 10-town seacoast area (residential). Public water systems are closely monitored to ensure safe drinking water. The United States Environmental Protection agency (EPA) established the Public Water System Supervision (PWSS) Program under the authority of the 1974 Safe Drinking Water Act (SDWA). Under the SDWA and the 1986 Amendments, the EPA sets national limits on contaminant levels in drinking water to ensure that the water is safe for human consumption. These limits are known as Maximum Contaminant Levels (MCLs) and Maximum Residual Disinfectant Levels (MRDLs). For some regulations, EPA establishes treatment techniques in lieu of an MCL to control unacceptable levels of contaminants in water. They also regulate how often public water systems (PWSs) monitor their water for contaminants and report the monitoring results to the states or to the EPA. Generally, the larger the population served by a water system, the more frequent the monitoring and reporting (M/R) requirements. In addition, the EPA requires PWSs to monitor for unregulated contaminants to provide data for future regulatory development. Finally, the EPA requires PWSs to notify their consumers when they have violated these regulations. The 1996 Amendments to the SDWA require consumer notification to include a clear and understandable explanation of the nature of the violation, its potential adverse health effects, and steps that the PWS is undertaking to correct the violation. Given the lack of a consistent drinking water source and the fact that the majority of drinking water was from public water systems, drinking water contamination seems unlikely to be contributing to RMS/PPB. Understandably, there is concern in the Seacoast area around emerging contaminants in drinking water, and while there is no evidence that water contamination has contributed to the RMS/PPB cancer cluster, there will continue to be interest and investigation into water quality issues on the Seacoast through the ongoing work of the Governor's Task Force and Legislative Commissions evaluating issues of environmental exposures and health.

Radiation exposure has also been expressed as a concern in the community. Only one individual reported close proximity to Seabrook Nuclear Power Plant. Three individuals reported "high" radon

levels in homes (one reporting mitigation), which has been associated with lung cancer in adults, but there is no evidence in the literature of an association between radon exposure and RMS. Additionally, all three individuals reporting higher radon levels lived outside the seacoast area. Aside from dental X-rays, which are common in children, only two individuals reported exposure to diagnostic medical X-rays.

Regarding other exposures, there were no exposures reported for illicit drugs either prenatally or by individual cases. There was also limited tobacco exposure with one person reporting second hand smoke exposure. None of the other respondents reported prenatal or individual case exposure to tobacco smoke. Evaluating exposure to prescription drugs did not reveal any common medications. Only two mothers reported use of prescription drugs during pregnancy, and these were different medications. There was also no consistent prescription medication reported taken by the individuals diagnosed with RMS/PPB, and most of the reported medications were common cold, anti-fever, allergy, or asthma medications. Additionally, no parental occupations were reported to suggest chemical exposures.

Based on our findings, there was not a common exposure identified to support moving to a case-control study. The scientific literature does not point to chemical or environmental exposures as a cause of RMS/PPB, and the majority of cases are thought either to occur sporadically, or be associated with a genetic predisposition or family cancer syndromes. The NH DHHS re-evaluated the number of RMS and PPB cases in the seacoast area in February of 2017 (one-year after the original report), and there have been no new cases of RMS/PPB identified over the last year in the 10-town seacoast area. We will continue to review and evaluate RMS and PPB cases reported to the NH State Cancer Registry as new data becomes available, and will reassess the need for ongoing monitoring over time.

While the findings of our investigation do not point to a common exposure among RMS and PPB cases, additional work is currently being performed in the Seacoast community to address ongoing concerns about environmental health. Specifically, it is anticipated that a Legislative Commission will be established to take over the work of the Governor's Task Force and ensure continuation of the investigation into potential environmental exposures and health. NH DHHS will continue to work closely with this Legislative Commission, elected officials, other government agencies, and the community to protect the health of the population and address health concerns. Additionally, in an effort to continue to address community concerns around cancer in the Seacoast area the NH DHHS is committed to the following:

- We will review new cases of RMS or PPB as they're reported to the NH DHHS, and at a minimum query the New Hampshire State Cancer Registry on an annual basis to identify new case of RMS or PPB in the 10-town area.

- We will continue to provide information to residents about cancer, and through the New Hampshire Comprehensive Cancer Collaboration (www.nhcancerplan.org) help to connect individuals diagnosed with cancer and their families to participate in ongoing cancer research to help improve knowledge about cancer prevention and treatment.

- We continue to be available to respond the public concern related to cancer in the Seacoast area and provide information about cancer prevention and control. Concerns or questions can be directed to: Whitney Hammond via phone 603-271-4959 or email whitney.hammond@dhhs.nh.gov

[i] Centers for Disease Control and Prevention. Cancer Clusters. [accessed: February 16, 2017]. URL: https://www.cdc.gov/nceh/clusters/

[ii] National Cancer Institute of the National Institutes for Health. Cancer Clusters. [accessed: February 17, 2017]. URL: https://www.cancer.gov/about-cancer/causes-prevention/risk/substances/cancer-clusters-fact-sheet#q4

[iii] Goodman, M., Naiman, J. S., Goodman, D., & LaKind, J. S. (2012). *Cancer clusters in the USA: What do the last twenty years of state and federal investigations tell us? Critical Reviews in Toxicology*, 42(6), 474–490. http://doi.org/10.3109/10408444.2012.675315

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