Protocol for Responding to Community Cancer Cluster Concerns

Texas Department of State Health Services
Environmental & Injury Epidemiology and Toxicology Unit
1100 West 49th Street
Austin, TX 78756
Phone: 1-800-588-1248
Fax: 512-776-7222

PURPOSE OF THIS DOCUMENT

This document details the Texas Department of State Health Services (DSHS) protocol for responding to community cancer cluster concerns. This protocol was adapted from the Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) 2013 *Guidelines for Investigating Suspected Cancer Clusters and Responding to Community Concerns* [1].

BACKGROUND

CDC and CSTE define a cancer cluster 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 [1].

In accordance with its mission, the DSHS Environmental Epidemiology & Disease Registries Section (EEDRS) is tasked with addressing community cancer cluster concerns, and has done so since 1984. Within EEDRS, the Environmental and Injury Epidemiology and Toxicology Unit (EIET) and Texas Cancer Registry (TCR) collaborate to respond to these concerns. Since 1995, TCR has been responsible for the collection, maintenance, and dissemination of high-quality Texas population-based cancer data. TCR meets national CDC timeliness and data quality standards, as well as North American Association of Central Cancer Registry certification standards.

Over the past 30 years, DSHS has responded to hundreds of inquiries about possible cancer clusters. Inquiries have come directly from citizens, as well as from other state and local government agencies. While some of the analyses conducted in Texas have identified statistically significantly higher-than-expected cancer, none have resulted in the identification of an association between environmental contaminants and the cancers observed. In fact, of all investigations of suspected cancer clusters conducted in the United States, few have been able to definitively identify a causal link with environmental exposures occurring in a community setting [2, 3]. However, cancer cluster investigations are important, as they provide concerned community members with data about the occurrence of cancer in their area.

The remainder of this document outlines the steps followed by DSHS in responding to community concerns regarding cancer clusters. The remainder of this protocol only addresses the response to concerns about cancer clusters in the community context. For concerns related to a suspected cluster in an occupational setting, please see Appendix A.

DSHS CANCER CLUSTER PROTOCOL

1   INITIAL CONTACT AND DATA COLLECTION

Purpose: To gather information from the concerned individual or group reporting a possible cancer cluster, and to provide education about cancer and cancer clusters.

1.1   Information Gathering

When report of a community cancer cluster concern is first received, DSHS collects additional information in order to determine the appropriate response. At a minimum, the following will be collected:

- Name, address, phone number, email, and organizational affiliation of the inquirer.
- Number and type(s) of cancer cases of concern.
- Geographic area of concern, including specific zip codes or census tracts.
- Time period of concern.
- Suspected exposure(s) of concern, and timeframe during which they may have occurred.
- Other government agencies previously or currently involved in responding to this concern, and the outcome of their involvement.
- How the inquirer learned of the possible cluster.
- Any other important details regarding the concern.

This information will then be entered into the DSHS cancer cluster inquiry database.

In addition to collecting information about the suspected cluster, DSHS will provide information to the concerned parties about cancer and cancer clusters, as well as the DSHS protocol for responding to such concerns. If the concerned individual wishes for DSHS to consider proceeding with a statistical analysis related to the cluster concern, he or she will be provided with next steps and an estimated timeframe within which a response will be provided. DSHS will provide information to the concerned parties about how a cancer cluster investigation is conducted and any potential limitations of the resulting data and study.

1.2   Determination of next steps

After initial information has been collected, additional information about the cancers and area of concern will be gathered and reviewed internally to determine appropriate next steps.

Factors that indicate a possible cluster include:
- The concern described could plausibly meet the definition of a cancer cluster.
- The cancers of concern are all of the same type or may share a common etiology. Frequently, not enough is known to rule out the possibility of a common etiology.
- The concern described involves a rare cancer or an atypical demographic distribution (such as breast cancer in men).
- There is a known or suspected environmental issue in the area of concern, and the literature supports an association between the environmental issue and cancer of concern.

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Factors that do not point to the existence of a cluster:
- Cancer cases occurred within genetically-linked family members (especially when cancers are known to be strongly genetically related).
- Reported cases include a few cases of a common cancer.
- Reported cases included many different cancers.
- The cases did not all live in the area of concern during the time during which they would have been exposed to a common carcinogen.

DSHS will review the concern and relevant additional data to determine if the inquiry may meet the definition of a cancer cluster, and whether an assessment of the occurrence of cancer is appropriate. Based on this review, DSHS will either:

➢ **Close the Inquiry**
If the concern clearly doesn't fit the definition of a cancer cluster (i.e. the concern involves many different types of common cancer), the inquiry will be closed. A follow-up email or letter will be sent to the concerned individual(s) summarizing the inquiry, and outlining next steps. If there are known or suspected environmental hazards in the area, additional information may be provided, such as appropriate contacts at environmental or other government agencies.

➢ **Proceed with an assessment of the occurrence of cancer**
At least one of following must be met in order to proceed with an assessment:

- The cancers of concern are all of the same type or may share a common etiology;
- The concern described involves a rare cancer or an atypical demographic distribution;
- There is widespread community concern.

The purpose of such an assessment is to determine whether the observed number of cases is statistically significantly greater than expected. It is not intended to identify the cause of the observed cancers or identify possible associations with any risk factors. If it is determined that an assessment of cancer can be conducted, a follow-up email or letter will be sent to the concerned individual(s) summarizing the inquiry, and outlining next steps.

2 ASSESSMENT OF THE OCCURRENCE OF CANCER

Purpose: To determine whether the observed number of cancer cases in the area of concern is statistically significantly greater than expected.

If DSHS has determined that an assessment of the occurrence of cancer is appropriate, the inquirer must submit a written request for the assessment to proceed. DSHS will then collaborate with the inquirer to confirm the cancers of interest, and the demographic, geographic, and temporal boundaries to be included in the investigation. These parameters will reflect the population the inquirer believes to be or have been at risk of a common exposure of concern, if known.

Before proceeding, DSHS will notify local or regional public health officials of DSHS's intent to conduct an assessment. DSHS will also notify elected officials and other state agencies as appropriate.

2.1 Data Sources

All cancer data will be obtained from the TCR. For each cancer type, the number of cases observed during the indicated timeframe and area included in the investigation will be calculated. For the same age range and timeframe, rates for each cancer for the state of Texas will be identified from TCR data. All-ages or adult cancers will be defined according to International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3), while childhood cancers will be defined according to the International Classification of Childhood Cancer (ICCC).

The census tract is the smallest geographic area that can be reliably analyzed. If the geographic area of investigation is defined by census tracts, census tract certainty will be calculated to determine proportion of cases that cannot be reliably coded to a census tract for reasons such as having a post office box address instead of a street address.

Population estimates for the area investigated will be calculated using linear interpolation based on population counts obtained from the United States Decennial Census, when possible. This method, outlined by the United States Census Bureau, assumes population growth has occurred in a linear manner [4].

2.2 Statistical analysis

To determine if a statistically significant excess of cancer exists in the area of investigation, the number of observed cancer cases will be compared to what would be expected for the area based on cancer rates in Texas.

Standardized incidence ratios (SIRs) will be calculated to determine if an excess of cancer exists in the area. The SIR is the number of observed cases compared to (divided by) the number of expected cases for each cancer type. The expected number of cancer cases will be calculated by multiplying the age-, sex-, and race-specific cancer incidence rates of Texas residents (reference population) by the number of people in the corresponding demographic groups in the area of investigation. Additionally, 95 percent confidence intervals (CI) will be calculated for the SIRs based on the Poisson distribution. If a 95 percent CI (range) includes 1.00, no statistically significant excess (or reduction) of cancer is indicated. If a 95 percent CI does not contain 1.00, the SIR is outside the expected range and is statistically significant.

The size of the SIR estimate indicates the magnitude of the difference between observed and expected cases. Larger SIRs are sometimes thought to indicate that it is more likely that there is a "real" cluster that can be studied. However, there is no specific threshold that constitutes a "large" or "small" SIR, and interpretation has to be context-specific. Recommendations for the interpretation of SIR effect sizes vary widely. For example, Neutra, *et al.*, suggest that an effect size of 20 might be an acceptable threshold indicating further investigation is warranted [5]. CDC and others suggest that a SIR of 10 might indicate the need for additional investigation [1]. Still others suggest that a "large" effect size is a ratio of about four [6, 7]. There is not a consensus on what effect size should be the threshold for concern.

For any cancer type with less than or equal to five observed cases for the time period included in the analysis, SIRs will not be calculated and case counts will be suppressed. Displaying case counts of less than six jeopardizes patient confidentiality. Furthermore, SIRs calculated with such small numbers are likely to be unreliable estimates. Although larger observed case counts may also result in unreliable SIR estimates, five observed cases is a threshold that balances statistical limitations with data transparency.

2.3   Determine Appropriate Next Steps

After completion of the assessment, DSHS will determine how to proceed, taking into consideration a number of factors. DSHS will consider the magnitude and direction (greater or less than one) of the calculated SIRs, along with additional details. For example, when using a 95 percent CI, 5 percent of SIR values calculated are expected to be statistically significantly higher or lower than the state average simply due to random chance. Therefore, if many different cancer types are evaluated in several geographic areas, the statistical issue of multiple comparisons must be taken into consideration. DSHS may also consider issues such as the number of observed cases, population growth and migration patterns in the area of investigation, and the rate of disease in the reference population.

Based on a review of relevant information, there are several possible next steps that may be recommended:

> **No further action needed.**
> If none of the cancers were statistically significantly higher than expected, DSHS may recommend no further action related to the assessment of the occurrence cancer. The investigation will be closed at this point.

> **Continue monitoring cancers in the area investigated.**
> If any SIRs were statistically significant, but SIRs were small, or estimates were not reliable due to small numbers, DSHS may recommend to continue monitoring cancer in the community by updating the cancer cluster assessment, upon request, as new years of data are completed in the TCR.

> **Assess the feasibility of conducting an epidemiologic study.**
> In considering the factors mentioned above, there is no single rule that applies to every situation. However, a recommendation to proceed with a feasibility assessment could be made under circumstances such as:

- SIRs are statistically significant and are greater than or equal to 10; and,
- There are enough cases to sufficiently power an epidemiologic study; and,

- There is a suspected or known environmental hazard in the area, and there is evidence in the scientific literature that this hazard may be associated with cancer.

2.4 Summary Report

DSHS will produce a summary report of the assessment. The report will include the following sections:

Executive Summary

Background
Pertinent information about the concern will be provided.

Methods
Specifies the data sources and statistical methods used in the analysis.

Results

A written summary of results as well as data tables will be provided.

Discussion
Provides detailed information on the limitations of cancer cluster assessments in general, and any additional limitations of the analysis conducted, including:
- Latency
- Residential history
- Multiple comparisons

Conclusions
A summary of the findings and guidance for the interpretation of these findings will be provided.

Recommendations and Next Steps
Recommendations and next steps to be taken by DSHS will be described.

Additional Information
Additional resources, such as facts about cancer risk factors, links to other cancer information resources, and DSHS contact information, will be provided.

2.5 Results Communication

The final report will be sent by letter or email to the concerned citizen(s) and relevant local officials, and posted on the DSHS website.

3   DETERMINING THE FEASIBILITY OF CONDUCTING AND EPIDEMIOLOGIC STUDY

Purpose: To determine the feasibility of conducting an epidemiologic study of the associations between specific cancers and environmental contaminants in the area investigated.

If DSHS recommends to proceed to this step, there are multiple factors that must be considered during the process to determine if an epidemiologic study of the associations between specific cancers and environmental contaminants is feasible. This process will be carried out transparently and in collaboration with the community, environmental agencies, and other partners.

3.1   Information Gathering

During the process of determining the feasibility of an epidemiological study, DSHS will gather additional information to be considered along with results of the previously-conducted assessment of cancer. This may include examination of any relevant existing data sources, such as additional clinical or environmental data.

➢ **Environmental exposures**
  DSHS will gather additional information about any exposures of concern identified by concerned community members. Existing literature, reports, and other documentation will be reviewed. DSHS will consult with other government agencies that may have knowledge of the area investigated.

➢ **Community concerns**
  DSHS will engage with community members to ask for input regarding what outcomes the community would like to see, and how those outcomes might be met.

➢ **Public health interventions**
  A list of public health interventions that may help achieve outcomes desired by concerned community members will be compiled. Interventions may include health risk assessments, cancer screenings, smoking cessation programs, or other targeted interventions.

3.2   Feasibility Assessment

Internal and external experts will be involved in assessing the feasibility of an epidemiologic study. An advisory committee comprised of subject matter experts may be comprised to address specific environmental, study design, statistical, or other issues. This group may include scientists with relevant expertise, including environmental protection specialists, toxicologists, epidemiologists, biostatisticians, and clinicians. Additionally, at least one community-designated representative will be included. DSHS will work with this group to determine if a follow-up epidemiologic study of the associations between specific cancers and environmental contaminants is feasible, and if it would be likely to identify the cause of the higher-than-expected cancer rates. Issues that may be considered during the feasibility assessment can be found in Appendix B.

As stated in the CDC and CSTE 2013 Guidelines:

> In some cases, despite the finding of a significantly elevated SIR, the feasibility assessment might indicate that further study will likely be unable to determine the cause of the elevated rate. In situations in which the types of cancers have no known association with an environmental contaminant, in which there are only a handful of cases, in which no suspected environmental

hazard exists, or in which other factors explain the observed cancer excess (e.g., a substantial movement of residents during the study period), investigators might determine that data are insufficient or that insufficient justification exists for conducting further epidemiologic study [1].

If a review of relevant information shows that additional study is not feasible, the investigation will be closed. If epidemiologic study is deemed feasible and likely to lead to the identification of associations between environmental contaminants and cancers, DSHS will proceed to coordinate necessary resources. The agency will most likely need to seek external funding, and may need to partner with external entities to complete the study. In either case, a summary document describing the feasibility assessment, final determination, and additional actions to be taken will be provided to community members and the public. If further epidemiologic study will be conducted, DSHS will work to ensure ongoing communication with the community throughout the process.

Appendix A.

Response to Occupational Cluster Concerns

DSHS does not currently have the appropriate data or resources to investigate occupational cancer concerns. Individuals concerned about potential exposures in the workplace will be referred to contact the National Institute for Occupational Safety and Health (NIOSH). Through its Health Hazard Evaluation (HHE) Program at program, NIOSH investigates concerns of hazardous working conditions when employers, authorized employee representatives, or employees request it. More information about the HHE Program is available at the NIOSH website at http://www.cdc.gov/niosh/hhe/, or by contacting 513-841-4382 or HHERequestHelp@cdc.gov.

Appendix B.

Feasibility Study Considerations

Environmental Exposures
- Are there any documented or suspected exposures to environmental contaminants?
  - Are there any known completed exposure pathways?
- Does the literature support a possible association between these potential exposures and the cancers with elevated SIRs?
- Would the dose and duration of exposure to any known contaminant be sufficient to make an association biologically plausible?
- Is the time sequence of exposure consistent with the latency period of these particular cancers?

Hypothesis
- Is there a testable hypothesis?

Study design
- What type of study would be appropriate to test this hypothesis?
- What cancer types/sites would be included in the study?
- What is the source population? How would the study population be selected? What would the inclusion criteria be?
- What sample size would be needed to conduct such a study?
- Is there an appropriate comparison group?
- What additional data (e.g. residential history, demographics, risk factors, exposures) would be needed to conduct a study?
- Can this data be obtained for both the cases and comparison group?
- Can environmental exposures be characterized accurately at the individual level?

Resource Requirements
- What resources would be needed to complete this study?
- Who will provide these resources?
- Is this the best use of these resources, or could they be used in other ways resulting in more benefit to the community?
- Who will lead the study?
- How long would this study take?
- What would the potential public health benefits of further study be?

Community Concerns
- What outcomes would the community like to see?
- What public health actions will contribute to the achievement of those outcomes?

References

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4.   US Census Bureau, *Methodology for the Intercensal Population and Housing Unit Estimates: 2000 to 2010*. 2012.
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