Investigation of Non-infectious Disease Clusters in Occupational Groups and Worksites

A disease cluster is the occurrence of more than the expected number of persons diagnosed with a certain disease within a specific group, a geographic area, or a period of time.

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Cancer/Cluster Analysis Work Group (CAWG)

Cancer Data Registry of Idaho (CDRI)
Idaho Hospital Association

Bureau of Communicable Disease Prevention
Bureau of Community and Environmental Health
Bureau of Vital Records and Health Statistics
Division of Public Health
Idaho Department of Health and Welfare

Idaho Department of Environmental Quality

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Introduction

Scope of this Document

Investigations of hundreds of reports of community cancer clusters over many years by numerous states have shown approximately 15 percent of reported cancer clusters to be real clusters, based upon statistical evidence. Cancer clusters of public health concern are those that represent a group of people who are at unusually high risk of cancer due to some factor or exposure that they have in common. A study of these clusters is sometimes necessary for the prevention of further cancers and to help understand more about specific risks for cancer.

Investigations of cancer in occupational settings have contributed critically to our understanding of cancer risks. About one third of the factors recognized as human carcinogens were first documented via worksite studies. Furthermore, it is estimated that 4-10% of cancers in the US are caused by occupational exposures. Central cancer registries are sometimes asked to respond to reports of disease clustering within occupational groups or worksites. In Idaho, the Cancer/Cluster Analysis Work Group (CAWG), with membership from the Cancer Data Registry of Idaho (CDRI), the Idaho Division of Public Health, and the Idaho Department of Environmental Quality, is responsible for responding to reports of cancer clusters. Understanding the reasons why the cancer risk is elevated may take several months, and the causes are not always resolved.

This document serves to inform CAWG of the procedures involved in the investigation of worksite cancer clusters. Additional procedures for responding to non-cancer worksite reports are included. This document provides a rough blueprint for an investigation but cannot prescribe exactly what to do in every situation. Consideration of the local resource base, including staff skills, and professional judgment at decision-making points need to be used in planning a response.

Use of the procedures alone cannot guarantee a timely resolution of the problem under investigation, nor will it guarantee finding an answer to why a cluster may be occurring in an area of concern. Other resources may be used to help determine the appropriate response, including:

- "Investigating Suspected Cancer Clusters and Responding to Community Concerns: Guidelines from CDC and the Council of State and Territorial Epidemiologists" (MMWR Recomm Rep. 2013 Sep 27; 62(RR-08):1-24), available at http://www.cdc.gov/mmwr/pdf/rr/rr6208.pdf

- "Guidelines for Investigating Clusters of Health Events" (MMWR July 27, 1990/Vol. 39/ No. RR-11), available at http://www.cdc.gov/mmwr/preview/mmwrhtml/00001797.htm.
- National Institute for Occupational Safety and Health. Occupational cancer. Washington, DC: National Institute for Occupational Safety and Health; 2010. Available at http://www.cdc.gov/niosh/topics/cancer.
- Brown AM. Investigating clusters in the workplace and beyond. Occup Med (Lond) 1999; 49:443–7.
  - "Cancer Clusters: A Toolkit for Communicators." A Collaboration of The Centers for Disease Control and Prevention and The National Public Health Information Coalition, September 2013. Available at: https://www.nphic.org/toolkits/cancer-cluster

Phases of the Investigative Procedure

The phases of a cancer or other non-infectious disease cluster investigation in the worksite are: Receipt of Report and Initial Evaluation (Phase I); Determining Feasibility of Conducting an Epidemiologic Study (Phase II); and Epidemiologic Study (Phase III).

A written report with a summary and conclusion(s) is then generated and reviewed internally by CAWG members, in a timely manner, before sharing with the inquirer initially reporting the cluster, the local public health district, and others deemed appropriate by CAWG. The decision to seek outside review, prior to distribution, is at the discretion of CAWG, and depends upon the availability of subject matter or methodological expertise from outside agencies.

Throughout the investigation, the lead investigator will be available to answer questions from the worksite contact, the public, and the media, and will draft press releases as needed for consideration by CAWG members, the Administrator for the Division of Public Health and the CDRI and IDHW public information officers.

Phase I: Receipt of Report and Initial Evaluation

Phase I is divided into two sections: Cancer Reports and Non-cancer Reports.

A. CANCER REPORTS

1. The public health epidemiology staff receiving the report of a suspected cancer cluster should complete the Cluster Form (Appendix A), which shall then be forwarded to the CDRI Epidemiologist. If a letter or email is received, it may be simply forwarded to CDRI. Alternatively, if a written request is received, it may be evaluated further to determine if the needed information is contained in the request.

CDRI Contact information:	Name:	Chris Johnson
	Email:	cjohnson@teamiha.org
	Phone:	208-489-1380
	Fax:	208-344-0180
	Mailing address:	615 N. 7th Street P.O. Box 1278 Boise, ID 83701
	Web site:	www.idcancer.org

2. The CDRI Epidemiologist will verify that the suspected cancer cluster is being reported by the worksite, and that related statistics are not previously published elsewhere. Reference materials such as a County

Cancer Profile and Cancer Cluster Fact Sheet will be provided to the inquirer. In instances where previous statistics have been already published, a written response will be given to the inquirer, with cancer fact sheets, statistical information, and other information as appropriate; additional information may be requested of the worksite contact as well.

3. An initial cancer case definition will be formed by the CDRI Epidemiologist, with possible input from the inquirer. The case definition will include:

    - Types of cancer and/or organ sites believed to be in excess
    - Location of index cases (place of work, area within worksite)
    - Time period of concern (for diagnosis of cases)
    - Suspected environmental worksite exposure(s) and likely period of exposures (if any)
    - Other risk factors (e.g., diet, infections, and family history)
    - Personal identifying information for cases (first name, middle name, last name, date of birth, sex, social security number, start and end dates of employment)
    - How the person learned about the suspected cluster

4. The CDRI Epidemiologist will make an initial judgment about the advisability of pursuing an inquiry into the suspected worksite cancer cluster, primarily based on whether the evidence presented fits the definition of a cluster and the biologic plausibility that the cancers could share a common etiology. A presentation of the suspected cluster will be made to CAWG, leading to a group discussion as to whether further evaluation is warranted, and determination of what additional information is needed to compare observed and expected cases of cancer or non-infectious diseases. CAWG shall document in a permanent log all information about the inquiry and the decision. Case verification for cancer will be performed by CDRI. To protect confidentiality, at no time during the case verification process, or thereafter, will individual-specific case data, including whether or not the reported case was confirmed as a cancer case, be shared with the inquirer, even if the inquirer initially provided personal identifying information for the cases.

    <u>The decision to close</u> the investigation at this point might require discussions with other CAWG members and/or additional subject matter experts, as well as multiple communications with the inquirer for possible additional data-gathering. If an inquirer is reporting an event that is not a suspected cancer cluster but rather one involving a known or possible environmental contamination, they should be referred to the Idaho Department of Environmental Quality and Bureau of Community and Environmental Health (Environmental Health Education and Assessment Program). If the inquirer is not satisfied with the decision to not pursue the investigation, CAWG shall provide a written explanation and include resources related to the decision.

    <u>The decision to pursue</u> the investigation shall prompt the CDRI Epidemiologist to notify the inquirer, explain what that entails and outline how CAWG will follow up with the inquirer and provide results. The CDRI Epidemiologist should ask the inquirer if there are others at the worksite (e.g., other workers with this cancer type) who would like to have a report on the results of the next step.

B. NON-CANCER REPORTS

1. The public health epidemiology staff receiving a report of a suspected cluster of non-infectious disease at a worksite should investigate the initial report as any other epidemiology investigation. If the public

health district staff feels that state epidemiology assistance is needed, they should contact the state Bureau of Communicable Disease Prevention at 208-334-5939.

2. Once initial information is gathered, the district (and state epidemiology teams, if needed) will develop an initial case definition. It may be necessary to contact the inquirer to develop the case definition. The case definition will include:

    - Disease or condition believed to be in excess
    - Location of index cases (geographic area, population group, place of work)
    - Time period of concern (for diagnosis of cases)
    - Suspected worksite environmental exposures and likely period of exposures (if any)
    - Demographic characteristics of cases

    Case verification for non-infectious diseases will be performed under the direction of the State Epidemiologist. To protect confidentiality, at no time during the case verification process, or thereafter, will individual-specific case data be shared with the inquirer, even if the inquirer initially provided the case names.

    The decision to pursue the investigation further, made by the local health district, involves considering the (i) concern from employers and employees, (ii) presence of worksite exposure(s) likely to cause the disease or condition, and (iii)presence, magnitude and trend of excess observed cases at the worksite. The Bureau of Communicable Disease Prevention (via the Chronic Disease Epidemiologist, State Toxicologist, and Environmental Health Program staff) has limited technical capacity to conduct preliminary worksite cluster investigations. A decision to pursue further investigation will also depend on the technical capacity of staff to conduct an in-depth investigation. If further investigation is warranted, resources available for local health districts to refer to include: the National Institute for Occupational Safety and Health (NIOSH) Health Hazard Evaluation Program (http://www.cdc.gov/niosh/hhe/), and the Idaho Occupational Safety and Health Consultation Program (http://oshcon.boisestate.edu/index.php?route=common/home). Please note that both of these evaluation services require referrals to come from employees and/or the employer of the worksite.

    The decision to close the investigation shall prompt a written report to be sent to the person who reported the cluster. If it is necessary to cease the investigation because of a lack of information from the inquirer, this should be communicated in writing with an offer to follow up if further information becomes available.

Phase II: Determining Feasibility of Conducting an Epidemiologic Study

The purpose of Phase II is to assess the feasibility of performing an epidemiologic study to compare the number of observed cases among the worksite cohort with expected numbers of cases from general population rates and/or examine the association between the cancer or non-infectious disease cluster and a particular environmental contaminant. If further study is feasible, an outcome of this step should include a recommended study design. All activities in this step should be carried out in collaboration with worksite partners and may also include community, environmental, and other partners. This step provides the opportunity to evaluate additional public health actions, such as smoking cessation programs, cancer screenings, health risk assessments, removal of environmental hazards, and/or other activities that should be conducted. If beneficial to public health, these actions should not be delayed pending the decision to conduct or complete an epidemiologic study.

The first actions in determining the feasibility of further study of the identified cluster include determining the study hypothesis and reviewing the scientific literature. Investigators should share information about time, cost, goals, purpose, and limitations of a potential study with all partners and carefully communicate realistic expectations.

Investigators must assess potential study design issues including sample size, a small case number, and study power. Experienced scientists with appropriate skills should be included in the investigative team. The investigative team may include an epidemiologist, a toxicologist, a physician, an environmental protection specialist, and representative(s) from the worksite to provide advice on the assessment as needed. It is necessary to identify such parameters as study population and its characteristics, including what descriptive, health, and risk factor data should be collected and determine the feasibility of obtaining the data. Investigators should:

- Confirm case diagnoses and determine which types of cancer or non-infectious disease, and which cases meet the case definition
- Identify a comparison group that, depending on the study design, does not have the disease of concern (i.e. a control group in a case-control study) or does not have the exposure of concern (i.e. unexposed group in a cohort study)
- Consider the willingness of persons to participate in interviews or studies for gathering data on health, possible exposures, the amount of time the affected persons have worked at the worksite of interest, occupation, and other relevant risk factors and confounding variables
- Verify whether the environmental contaminants of concern are known carcinogens, consider possible and plausible routes of exposure, ascertain whether or not cases were exposed to an environmental contaminant in sufficient doses and for a sufficient time to make the association biologically plausible, and consider if the time sequence of exposure is consistent with the latency period and the causation of the cancers of interest
- Determine whether residential and occupational histories for affected persons are obtainable
- Determine if it is possible to characterize exposure to suspected environmental hazards accurately at the individual level and in a way that reflects the period of concern

It is not recommended to engage in a general, open-ended inquiry to identify potential contaminants in a worksite, in the absence of a suspected etiologic agent. Investigators should identify study design requirements and available resources to conduct the study. This process includes identifying the scope of the study and determining whether sufficient resources and data are available to complete meaningful work. Investigators should:

- Determine which parameters to use for geographic scope, study timeframe, and demographics and select a timeframe that allows for sufficient latency in cancers of concern
- Determine the study design, sample size, and the statistical tests necessary to study the association as well as the effect of a smaller sample size on statistical power
- Determine the appropriateness of the plan of analyses, including hypotheses to be tested as well as epidemiologic and policy implications, and
- Assess resource implications and requirements of the study and identify sources of funding

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 may explain the observed cancer excess (e.g., cases diagnosed among newly hired workers), investigators might determine that data are insufficient or that insufficient justification exists for conducting further epidemiologic study.

If the feasibility assessment suggests that little will be gained from proceeding further, the investigator should close the inquiry and summarize the results of this extensive process in a report to the inquirer and all other concerned parties. In some circumstances, the worksite, public, or media might continue to demand further investigation, regardless of cost or biologic plausibility. Working with established worksite relationships, media contacts, and the advisory panel will be critical in managing and responding to expectations. If an extensive epidemiologic investigation is not carried out, it is critical to establish other possible options to support worker health, depending on the information and resources available.

If the feasibility assessment suggests an epidemiologic study is warranted, further outreach, health assessment, interventions, or other public health actions also might be appropriate. Conducting epidemiologic investigations can take several years; the health agency should consider what can be done in the interim to help protect the community's health and keep its members informed. This level of investigation often can be seen as research rather than public health response to a worksite concern. Providing periodic progress reports to keep the worksite involved can help overcome this perception.

Phase III: Epidemiologic Study

This step involves a standard epidemiologic study that compares the number of observed cases among the worksite cohort with expected numbers of cases from general population rates and/or tests a hypothesis of the association between putative exposures and specific non-infectious disease or cancer types, for which all the preceding effort has been preparatory. Using the feasibility assessment as a guide, responders should develop a protocol and implement the study. The epidemiologic study will, at a minimum, be used to collect additional exposure history information about cases, and may include a case-control study, a cohort study, other study designs and possibly environmental sampling. The planning and implementation of such a study will be performed by members of CAWG with leadership by the State Epidemiologist, the district health departments, federal partners such as ATSDR, or the CDRI Epidemiologist, depending on the type of disease or condition of concern, and the complexity of the study. CAWG will engage the worksite in the selection of members to participate in the investigation that shall include a lead contact for the worksite and may include the local public health district and membership from the local medical community.

It is acknowledged that an investigation can augment the existing fear and uncertainty in the worksite brought on by the perception that a suspected disease cluster exists, which might have negative social and economic impacts.

Epidemiologic studies are dependent upon the availability of funds and staff for proper implementation. Multiple barriers may exist which must be examined and overcome in order to proceed further. These include:

- Persons identified as part of a cluster may be deceased, missing, or reside or work outside of Idaho and therefore unable to provide a detailed exposure history and/or disease information
- Persons identified as part of a cluster may be unwilling to participate in a survey or health study
- Federal assistance (e.g., EPA, ATSDR, CDC) in terms of technical expertise, funding, and laboratory testing, is time-intensive to procure, or may not be available
- Privacy and confidentiality of all persons in the possibly affected worksite, and former employees, must be respected

- Collection and testing of environmental samples may cause significant delays

Demonstrating a statistically significant association does not prove causation, and often relies on clinical and laboratory studies. Even if a disease cluster is identified and environmental contamination is identified, an investigation might not demonstrate a conclusive association between the two. Other risk factors (e.g., smoking, personal behavior, and genetic traits) should also be explored. Conversely, even if the investigation does not identify an association, the exposure still might be linked to the cluster; however, in such a case more scientific information might be required (e.g., toxicological and clinical data) to establish an association. Epidemiologic studies alone often are not able to detect small effects, particularly in small populations or when the number of cases is limited.

1. Verification of "Index" Cases

   In many instances, the illness allegations are not supported by medical records. And sometimes, reported cases occurred in persons who developed the illness prior to employment and therefore should not be counted. Cases reported as a particular type of cancer may be found, when verified, to be several different types of cancer or not cancer at all. For all these reasons, it is necessary to verify cancer cases and cases of non-infectious diseases using other sources of data, including worksite employee rosters, physician records, hospital records, and vital records. The availability of information about specific health problems can be limited because of confidentiality and access to such records.

   Case verification for cancer will be performed by CDRI. Case verification for non-infectious diseases other than cancer will be performed under the direction of the State Epidemiologist. Full case ascertainment means finding all additional unreported cases of the disease in question which occurred in the location during the time period of interest and meet the case definition. One investigation option comprises CDRI reviewing a list of cancer cases among current and/or former worksite employees, and matching to the CDRI database to confirm cancer primary site and other information. This option allows for comparison of the primary site distribution among the employees to the general cancer population, but would not be suitable for statistical assessment of the existence of a cancer cluster. The second, more robust, option comprises CDRI matching the employee roster against the CDRI database. This second option would facilitate statistical assessment of the existence of a cancer cluster. For the second option, in order to conduct the linkage between the employee roster and the CDRI database, CDRI would request the following fields: first name, middle name, last name, date of birth (at the least, month and year), sex, home and/or employment address, social security number, and start and end dates of employment. For occupational rather than employee cohorts, license type/status (i.e., active, inactive, or historical), dates of license original issue and expiration, and latest year of license recertification, are also necessary.

2. Comparison of Observed and Expected Numbers of Cases

   i. Selection of Comparison Group

   As a first step, selection of the exact area of concern (e.g., one or several buildings in a worksite, a geographical area where an occupational cohort practices, etc.) and selection of the area with which it is to be compared must be determined. The comparison area may be the state of Idaho, the county in which the worksite is located, and/or the national cancer rates in the registries comprising the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (SEER). Selecting additional characteristics within the comparison group, such as high or low socioeconomic status, may offer more

comparable reference rates of illness with which to compare the observed cases. The expected number of cases will generally be calculated based upon age-specific and sex-specific rates for the state of Idaho during the same time period as the reported cluster. These rates will be multiplied by person time for the worksite cohort to calculate the number of expected cases.

ii. Data Management

Certain initial data cleaning steps may be necessary to perform on the dataset from the worksite or occupational cohort group of interest, before linkage with the CDRI population-based cancer registry. Link Plus, a probabilistic record linkage program developed at CDC's Division of Cancer Prevention and Control in support of the National Program of Cancer Registries (NPCR) (http://www.cdc.gov/cancer/npcr/tools/registryplus/lp.htm) may be used to detect duplicate records in the worksite or occupational cohort group of interest. Accurint, an online public records service (http://www.accurint.com) from LexisNexis may be used to populate missing data such as dates of birth and changes of residence among former workers. Additionally, a file of name frequencies by sex from the National Center for Health Statistics can be used to impute values for sex, if that information is not provided in the dataset from the worksite or occupational cohort group of interest. If the percent a name is associated with female sex is between 45–65% (i.e., "Pat"), further research should be conducted to assign the proper sex to the individual.

iii. Linkage

Linkage between the worksite or occupational cohort group of interest and the CDRI population-based cancer registry can subsequently be performed using Link Plus, where probabilistic record linkage scores are computed based on the theoretical framework developed by Fellegi and Sunter (*Fellegi IP, Sunter AB. A theory for record linkage. Journal of the American Statistical Association 1969; 64:1183–1210*). Decisions such as whether to include in the person linkage only the most recent cancer case or every cancer case regardless of year of diagnosis for each person need to be made prior to linkage. During linkage, records can be blocked on birth date, social security number, and Soundex (http://www.archives.gov/research/census/soundex.html) functions using last name, first name, and middle name. Among the candidate matching pairs, match scores will be computed using last name, first name, middle name, social security number, and birth date. Upon linking the two datasets, careful manual review of the resulting analytic dataset should be made.

iv. Person-time Contribution

Finally, vital status and/or date of last contact should be determined in order to inform the person-time contribution of each person. The Social Security Death Index (http://www.ntis.gov/products/ssa-dmf.aspx) may be used to help ascertain fact and date of death among any deceased employees. Because CDRI was not population-based until 1971, cancer cases and person-time at risk should not be counted prior to 1971 in the resulting analytic dataset. This may result in the exclusion of a number of cancer cases in the original employee or occupational cohort dataset, since they have not been ascertained as true cancer cases as per the registry. To compile person-time, the clock should start at either their initial or latest date of hire/licensure (censored to 1971). Additionally, the end of the study period should be the latest date for which CDRI can be reasonably sure that all cases in the cohort have been reported to CDRI. Moreover, cancer latency periods need to be addressed, if pertinent to the investigation. If a latency period is assumed, cancer cases and person-time at risk will be accrued starting at a pre-determined time point equal to the latency time period after the start of the study

period (usually the date of hire at the worksite or licensure for the occupation of interest). This assumes that no case diagnosed within the latency period could be related to a worksite hazard. Cancer latency periods are typically assumed to be long (http://www.cdc.gov/niosh/topics/cancer/clusters.html, http://www.ncbi.nlm.nih.gov/books/NBK12622/). If a person ended employment prior to the end of the study period, cancer cases and person-time at risk should still be accrued until the end of the study, given that the person still had the potential exposure of interest. A mock-up of case and person-time contributions is shown in Figure 1.

Figure 1. Examples of Case and Person-Time Contributions to a Worksite or Occupational Cohort Cancer Cluster Investigation.

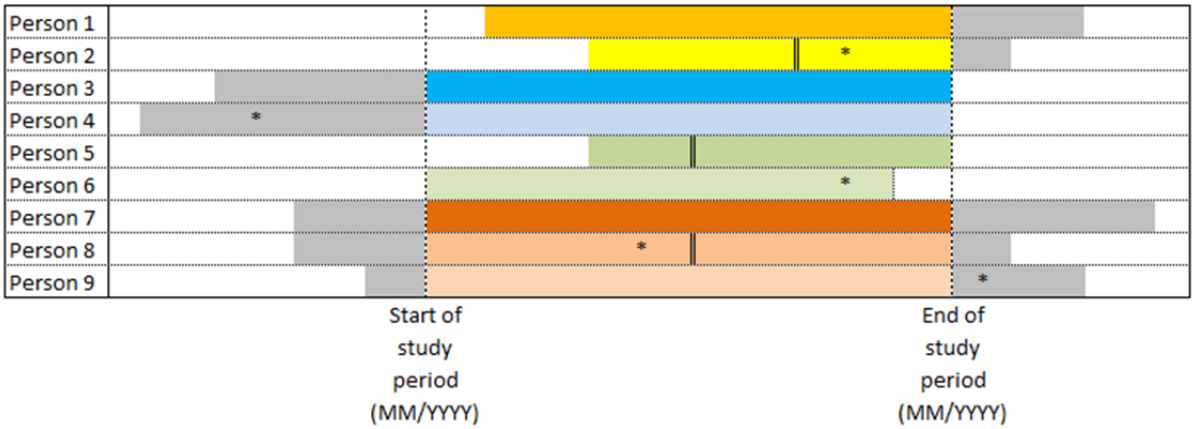

Figure 1. Mock-up data are for illustration purposes only and not sourced from any analytic dataset. Asterisk (*) indicates cancer diagnosis. Grey bars indicate no contribution to person-time. Persons 2, 6 and 8 would each contribute cases to the investigation, as denoted by asterisks. Persons 1, 3, 4, 5, 7 and 9 would contribute person-time, but not cases (no cancer diagnosis). Aside from person 6, who died shortly before the end of the study period, each person would contribute person-time up until the end of the study period, even if they left employment sometime between the start and end of the study period (i.e., persons 2, 5 and 8; denoted by double vertical lines). Person 9 would not contribute to the case count because the cancer diagnosis occurred after the end of the study.

v. Analyses

SAS (Statistical Analysis System) is a software suite developed by SAS Institute (Cary, NC) for data management and advanced analytics (http://www.sas.com/en_us/home.html). A SAS program can be used to create an analytic dataset, with custom variables appropriate to the particular study (i.e. city, county, and health district), and the dataset will be analyzed using SEER*Stat software (www.seer.cancer.gov/seerstat). If a sensitivity analysis is desired, additional analytic datasets may be created with the modified parameters of interest. For example, several analytic datasets with differently accrued person-time calculations may be created to examine the sensitivity of results to assumptions regarding follow-up of former employees.

Standardized incidence ratios (SIR) and p-values will be calculated for tests of observed versus expected numbers of cases using the SEER*Stat MP-SIR session. An SIR <1 indicates that there are fewer cases than expected based on reference rates, while an SIR >1 indicates that there are more cases than expected, and an SIR = 1 means that the numbers of observed and expected cases are equal. Results will typically be tabulated using CDRI annual report primary site categories (see www.idcancer.org).

3. Written Report

Written results will be sent to the lead contact for the worksite. For cancer cluster investigations, the CDRI epidemiologist or designated Division of Public Health epidemiologist will write the report and include, as an attachment, a Cancer Cluster Fact Sheet. For other non-infectious diseases, the district epidemiologist, State Epidemiologist or other principal investigator will be responsible for writing the report. A draft will be submitted to CAWG members and the Division of Public Health Administrator. A period of one week (5 working days) will be allowed for review. After comments are incorporated into the report, a final copy will be submitted to the inquirer, all CAWG members, and the Division of Public Health Administrator. If the results of the inquiry show no excess, the cluster investigation is considered closed unless continuing concern is high; in this case, CAWG will discuss whether further action is needed.

Reported clusters will, upon investigation, fall into three categories:

No excess. This occurs when the observed number of cases for a worksite is less than or equal to the expected number of cases, based on general population reference rates. This also occurs when the observed number of cases is numerically greater than the expected number of cases, but not statistically significantly different from the expected number of cases (i.e., p-value ≥ 0.05 or 95% confidence interval [CI] crosses 1.0).

Explained excess. Based upon experience to date in many states, concerns regarding non-infectious disease clusters arise because the public is not aware how common these conditions, such as cancer, spontaneous abortion, and birth defects are. For example, an excess of lung cancer in a worksite with a high percentage of smokers and no unusual environmental exposure is not likely to constitute a cluster. Typically, worker concern subsides when they are adequately informed of the issue.

Unexplained excess. In some instances, however, the inquirer's concerns are confirmed. The number of cases may be more than expected based upon comparison rates (observed cases statistically greater than expected cases: $p<0.05$ or 95% CI>1.0), indicating that the concern warrants further investigation

An important consideration is the issue of practical versus statistical significance. If observed and expected case counts are large enough, minor differences are more easily detected and may be statistically significant. However, this difference may be of little practical or clinical significance (e.g., a difference of 1% in a disease rate). Furthermore, rates based upon small numbers (i.e., fewer than 10 cases) are subject to substantial random variation. If the number of infant deaths in a county increased from 1 in 2014 to 2 in 2015, and the number of births remained approximately constant, looking at the infant mortality rate would erroneously suggest that the problem had become twice as great. Examining the numbers behind rates is always a good idea, and in some cases just looking at the numbers makes more sense.

To address the problem of rates based on small numbers, all communications containing rates or percentages should include a caution about interpretation. An example is: "Rates based upon 10 or fewer cases (numerator) should be interpreted with caution, since they may vary greatly over time." In addition, a small cell suppression rule will be invoked to not present statistics when the number of cancer cases is less than 5, unless at least 5 years of data are aggregated. This rule will hold for statistics for all cancer sites combined and for individual primary sites. The rule may be disregarded with CAWG

approval, such as in circumstances when rare diseases and conditions generate small numbers of cases that may be important for public health.

APPENDIX A

Idaho Cancer and Non-Cancer Cluster Investigation
Initial Inquiry Report Form

Inquirer Information

First Name Last Name Phone Number

Street Address City State Zip

E-mail Address

Affiliation of the Inquirer:

☐ Concerned citizen ☐ Private physician
☐ Employer representative ☐ Other _____ (specify)

Area of Concern

Where has the reported cluster occurred (which workplace, occupational group, city, county, neighborhood, etc.)?
Does the inquirer suspect a specific environmental exposure?

What is the time period during which people became ill?
What types of illnesses are being reported?
How many people (list ages, if known) are reported with illness?

If concern involves cancer, fax this form to: CDRI: fax 208-344-0180

Appendix B: Talking Points on Clusters and Cluster Fact Sheet

Here are some points which might be helpful when talking with a caller concerned about a disease cluster:

- Usually clusters occur by chance alone and are not related to a specific exposure. That is to say, each case in the cluster probably has a different cause, even though the cases have clustered together in time and/or space.

- It's difficult to reconstruct exposure histories. This is especially true for diseases with long latency periods between exposure to a disease-causing agent and the onset of disease symptoms. What's in the air or water today may not be what was in the air or water several years or decades ago.

- It's difficult to detect subtle effects, especially when the number of cases is small. If the relationship were strong, we may have seen an association in other places, such as workers, where exposures are higher.

- For diseases of unknown etiology, we often don't know what to look for as a possible cause, unless there is a unique exposure of concern.

Regarding Cancer

- Cancer is a term for a group of more than 100 different diseases in which abnormal cells divide without control and can invade nearby tissues. Cancer is very common: about 1 in 2 men and 1 in 3 women will be diagnosed with cancer sometime in their life. About 1 in 4 deaths in the US is attributable to some form of cancer. Cancer is the leading cause of death in Idaho.

- The causes of many types of cancer are unknown.

- Cancer is almost always caused by a combination of factors that interact in ways that are not yet fully understood.

- Cancer is more likely to occur as people get older; because people are living longer, more cases of cancer can be expected in the future. This may create the impression that cancer is becoming much more common, when an increase in the number of cases of cancer is partly related to the aging of the population.

- There are many different types of cancer, which are caused by a wide variety of causal mechanisms. A variety of diagnoses speaks against a common origin.

- A cancer that spreads to another part of the body should not be considered a new case of cancer. For example, if a breast cancer spreads to the lung, this is not considered to be a new lung cancer.

- Some types of cancers may occur anywhere in the body. They should not be classified according to where they appear in the body. For example, non-Hodgkin lymphoma may manifest itself in the brain, but it is not brain cancer.

- Cancer involves a series of changes within cells that usually occur over the course of many years. More than 10 years can go by between the first cellular abnormality and the clinical recognition that cancer is present, which often makes it difficult to pinpoint the cause of the cancer.

Regarding Birth Defects

- Major birth defects occur in 1%–2% of live births.
- The causes of most birth defects are unknown.

Useful Information for Reducing the Risk of Chronic Diseases

- Don't smoke or chew tobacco.
- Eat at least 5 servings per day of fruits and vegetables.
- Limit the amount of fat — especially saturated fat — in your diet.
- Exercise regularly — one hour each day.
- Limit alcohol intake.
- Protect yourself from sunburn.
- Follow recommended guidelines for preventive services and screening for early detection and treatment, such as screening for colorectal, cervical and breast cancer, high blood pressure and high cholesterol.

Useful Websites for the Consumer

National Cancer Institute, "Cancer Clusters":
http://www.cancer.gov/cancertopics/factsheet/Risk/clusters

CDC Cancer Web site: http://www.cdc.gov/nceh/clusters/

CANCER CLUSTER FACT SHEET

Cancer is a term that includes more than 100 different diseases, each characterized by the uncontrolled growth and spread of abnormal cells. A CANCER CLUSTER is the occurrence of a greater than expected number of cases of cancer within a small area or within a short period of time.

Cancer is one of America's greatest public health concerns. Nearly one in two men and women in the United States will be diagnosed with cancer sometime in their life. Cancer is the second leading cause of death in the United States. In Idaho, cancer accounted for about 22 percent of deaths in 2013, and was the leading cause of death. When someone is diagnosed with or dies from cancer, family, friends, and neighbors sometimes learn of other cases of cancer in their community. This apparent clustering of cancers is often reported to health departments or the media. However, closer inspection usually reveals that these "suspected" clusters involve several different types of cancer among persons of different ages, sexes, and occupations. A “real” cancer cluster will usually involve one type or site of cancer.

When several cancers occur within a limited area, this may represent a real cluster, but it may not be the result of an increased community risk of cancer. For example, in Idaho there are 44 counties and every year, about half of the counties have rates of cancer that are above the average county value, and about half have rates that are below the average value. Counties may have above average rates one year and the next year the same counties may have rates below the average. This variation is expected and is more pronounced as the population being studied gets smaller (county, city, ZIP Code, neighborhood). Investigations of hundreds of reports of cancer clusters over many years by numerous states have shown approximately 15 percent of reported cancer clusters to be real clusters, based upon statistical evidence.

Cancer clusters that are a public health concern are the ones that represent a group of people who are at unusually high risk of cancer due to some factor or exposure that they have in common. A study of these clusters is sometimes necessary for the prevention of further cancers and to help understand more about specific risks for cancer. Understanding the reasons why the cancer risk is elevated may take months or longer, and the reasons are not always resolved. Less than 5 percent of all cluster reports fall into this category of a meaningful cluster.

Cancer cluster investigations require data on the total number of residents and the number of diagnosed cancer cases in the area to be reviewed. At present time, the Cancer Data Registry of Idaho is able to investigate cancer incidence for several levels of geography: county, ZIP code, and census tract.

For more information regarding cancer clusters, contact:

Cancer Data Registry of Idaho
615 North 7th
PO Box 1278
Boise, Idaho 83701
(208) 489-1380
www.idcancer.org