

# **Cancer Inquiry Guidelines**

## **Manual for Investigating Potential Cancer Clusters in Missouri Communities**

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# Abbreviations

## Missouri Department of Health & Senior Services

BCCDC .....	Bureau of Cancer and Chronic Disease Control
BEE.....	Bureau of Environmental Epidemiology
BHI.....	Bureau of Health Informatics
BVS.....	Bureau of Vital Statistics
BRFSS.....	Behavioral Risk Factor Surveillance System
CCCP.....	Comprehensive Cancer Control Program
CHSI .....	Section for Community Health Services and Initiatives
CLPHS .....	Center for Local Public Health Services
DHSS .....	Missouri Department of Health and Senior Services
EPH .....	Section for Environmental Public Health
EPHP .....	Section for Epidemiology for Public Health Practice
HPCDP .....	Section for Health Promotion and Chronic Disease Prevention
MCR .....	Missouri Cancer Registry
MICA .....	Missouri Information for Community Assessment
OOE .....	Office of Epidemiology
OPI .....	Office of Public Information

## Other State Agencies

MDNR .....	Missouri Department of Natural Resources
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## Federal Agencies

ATSDR .....	Agency for Toxic Substances and Disease Registry
CDC .....	Centers for Disease Control & Prevention
EPA .....	Environmental Protection Agency
NIOSH .....	National Institute of Occupational Safety and Health
NCHS .....	National Center for Health Statistics
NPCR .....	National Program of Cancer Registries
OSHA .....	Occupational Safety and Health Administration

## Additional Abbreviations/Acronyms

CI .....	Cancer Inquiry
LPHA .....	Local Public Health Agency
MoSTRA .....	Missouri State Tumor Registrars Association
MSA .....	Metropolitan Statistical Area
NAACCR .....	North American Association of Central Cancer Registries
SEER .....	Surveillance, Epidemiology, and End Results Program
U.S. ....	United States

# Introduction

## Purpose

The purpose of the *Cancer Inquiry (CI) Guidelines* is to assure a useful, cost-effective, and scientifically sound process to investigate potential cancer cluster concerns. This document provides Department of Health and Senior Services (DHSS) staff a systematic, scientific and prompt way to respond to concerns about possible excess cancer in a community, to ensure the public has been provided with general information about cancer and to inform the public about what the cancer data in the reports means to their communities. The guidelines provided in this manual are based upon the understanding that most identified cancer excesses are not related to environmental causes, but instead are due to normal random variation in cancer occurrences, or to personal behaviors, genetic causes, or unknown factors. They are also based on the knowledge that epidemiological investigations conducted to identify the source of the excess cancer often have little chance of determining a definitive cause. The manual does not cover every possible situation or variable which may arise during a cancer inquiry. In some cases, direction and actions will be determined by the best judgment of the appropriate involved professionals.

## Cancer Inquiry Process Overview

The major focus of the CI process is to work with individuals or communities in exploring the nature of their cancer concern, provide health education on cancer and lifestyle risk factors and, when appropriate, provide epidemiological information. DHSS staff members, in consultation with the Chronic Disease Public Health Epidemiologist and the CI committee, work with communities in need of education. Staff or regional cancer coalition members may give educational presentations in locations with a cancer concern and may help to address the specific needs of that community. As part of this process, staff communicates with Local Public Health Agencies (LPHA) to coordinate, educate and review cancer rates and risks.

The CI process focuses on determining if a perceived excess is real. If a true cluster is identified, the CI staff will assist in the implementation of epidemiological studies, notify agencies responsible for remediation of the environmental hazard (if one exists), and educate residents in the area of concern regarding the risk(s) and the response of state government and other agencies concerning cancer in their community. Rarely is it necessary to refer the identified environmental health hazard(s) for control or eradication.

DHSS also serves as a gateway for referral of environmental, regulatory and health concerns. For example, if a community is found to have excess mortality from breast cancer, residents may be referred to the Show Me Healthy Missourians project to increase screening efforts. A complaint about pesticide use may be referred to the Missouri Department of Agriculture. Once an inquiry is complete, a DHSS staff member communicates the inquiry results concerning the perceived cancer excess to the inquirer and, when appropriate, the community involved.

DHSS has created and maintains a confidential database that aggregates information about each cancer concern and inquiry. Examples of information contained within the database are: demographics, geographic location(s) and actions related to a CI. Upon completion of the CI, patient information and correspondence is archived according to DHSS confidentiality policies.

## Investigation Tools and Resources

DHSS uses a cancer surveillance system to determine whether there is an increase in cancer incidence and/or mortality. Surveillance data can confirm increases in cancer incidence or mortality, but it cannot definitively point to the cause of the increase. Questions related to cause are better addressed by systematic epidemiological studies.

Since the 1970s, when a number of state cancer registries were established, many public health scientists and individuals have hoped that the study of anecdotal observations of clusters of cancer in the community might lead to prevention of new cases by the discovery of specific causes of these cancers. Since then, thousands of investigations have taken place throughout the country, mainly conducted by state, local or federal agencies. With few exceptions, none of these investigations have led to the identification of definitive causes of any of these possible clusters, even when a statistically elevated number of cancers in a geographic area could be documented.

The principal data source for the CI process is the Missouri Cancer Registry (MCR), currently housed under contract to the University of Missouri. MCR receives data (patient demographics,

tumor characteristics and treatment information) from hospitals and other mandated reporting sources statewide; these data are used for case verification, case ascertainment, and incidence rate calculations. MCR was established in 1972 when a dozen hospitals began voluntarily submitting inpatient data. MCR did not become a population-based registry until 1985 following enactment (August 1984) of a State statute requiring hospitals to report cancers diagnosed in an inpatient setting. MCR has been a recipient of National Program of Cancer Registries (NPCR) funding since 1995 and is required to adhere to guidelines established by the Centers for Disease Control and Prevention (CDC). MCR's data not only meet, but exceed NPCR requirements; in addition, MCR is a North American Association of Central Cancer Registries (NAACCR) Gold-certified registry. The registry's NPCR reference year and the earliest year of high-quality data is 1996. Cancer reporting was expanded in 1999 to include hospital outpatient settings, physician offices, pathology laboratories, ambulatory surgical centers, residential care facilities and assisted living facilities, intermediate care facilities, skilled nursing facilities and free-standing cancer clinics and treatment centers (192.650-192.657 RSMo; (see <http://mcr.umh.edu/mcr-aboutmcr.php> for more details).

Other data sources that may be evaluated during the CI process include the Missouri Information for Community Assessment (MICA) interactive health data system, death certificates, Behavioral Risk Factor Surveillance System (BRFSS), the Patient Abstract System and cancer case listings. MICA is an interactive system on DHSS' website that allows users to create tables or maps displaying data on public health topics such as deaths, hospitalizations and cancer cases (<http://health.mo.gov/data/mica/MICA/>). The BRFSS, a state-based system of telephone surveys sponsored by CDC, collects information on chronic health conditions, health-related risk behaviors, use of preventive services and health care access from adult Missouri residents (age 18 or older). Established through enactment of 192.665-192.667 RSMo in 1993, the Patient Abstract System, Missouri's hospital discharge database, contains both inpatient and outpatient data. Data from special surveys, such as the Missouri County-level Study, may also be evaluated. Additional current reference materials may also be used in this process.

## **Communication Plan**

At every level of the inquiry process, CI staff members, in consultation with the State Epidemiologist, prepare a report that contains recommendations for action. Should questions arise at any point throughout the process, attorneys in DHSS' Office of General Counsel may be consulted.

When needed, DHSS' Office of Public Information (OPI) may be notified of an inquiry being conducted. OPI staff may serve as consultants and assist in implementing various communication methods as needed throughout the CI process. A written communication plan designating the responsibilities of staff may be required for high profile inquiries.

The CI Committee meets quarterly to review active concerns and inquiries. The CI Committee guides staff actions in proceeding with the inquiry. Details of this process are further explained in the section on "Committee Responsibilities"

When appropriate, correspondence with inquirers is copied to those within DHSS who may be involved in the inquiry, such as the Section for Environmental Public Health or the Center for Local Public Health Services (CLPHS). The appropriate LPHA and any other agency involved with the process may also be copied.

Once an inquiry is complete, DHSS staff members, sometimes assisted by MCR staff, prepare a final report on the issue. Results of some inquiries may be conveyed through public meetings and news releases as well as by direct mail to the inquirer. De-identified copies of this report may be made available to the public, e.g., by posting on DHSS' website. The DHSS website is also used to inform inquirers about the process and for access by other agencies and researchers.

## **CI Guidelines Summary**

This document is a systematic approach for decision-making, based on the basic principles of epidemiological reasoning and causation. Upon initial contact from an inquirer, the DHSS Comprehensive Cancer Control Program (CCCP) manager determines if it is a cancer information request or a concern. A concern becomes an inquiry when the CI Committee determines the need to proceed to a higher level of investigation. All cancer inquiries begin at Level 1 of a three-level process. Each level uses epidemiological reasoning and/or statistical tests to determine if the inquiry should proceed to the next level.

At each level, the CI Committee reviews documentation, findings and/or recommendations for further action. The CI Committee accepts, rejects or revises the recommendations. Then, DHSS staff coordinates the implementation of approved recommendations.

## Oversight

The **CI Program** is jointly chaired by the administrators of the Sections for Community Health Services and Initiatives (CHSI), Environmental Public Health (EPH) and Epidemiology for Public Health Practice (EPHP). The program is staffed by means of collaboration between various offices within DHSS and the Missouri Department of Natural Resources (MDNR). The CI Program is located in the Division of Community and Public Health, Section for Community Health Services and Initiatives, Bureau of Cancer and Chronic Disease Control (BCCDC).

## Staff

The **Chief of BCCDC** provides oversight to all cancer programs as well as the CI Process.

The **CCCP Manager** coordinates and facilitates contacts; serves as liaison with collaborating agencies; provides direction and coordination of educational efforts; refers environmental threat responses to the Bureau of Environmental Epidemiology (BEE); and establishes and maintains communication channels with residents and other members of the public involved in cancer inquiries. In addition, the Manager updates the BCCDC Chief regarding all new inquiries, and directs daily operations of the CI Program in collaboration with the epidemiology and research staff. The CCCP Manager also provides a main point of contact for all cancer concerns. This staff person gathers information from the concerned individual(s) and begins the process of investigation if the individual seeks to determine if the environment is the cause. All communication is tracked until the CI Committee determines the case should not proceed to an inquiry level or the CI is complete and resolved.

**BCCDC staff** work with research and Office of Epidemiology (OOE) staff in the department who provide epidemiological consultation on potential cancer cluster occurrences. This consultation assures the use of epidemiological criteria and reasoning, as well as the application of a systematic method(s) to evaluate potential cancer clusters, supervision of the process of case verification and ascertainment, design and implementation of feasibility studies and final reporting with recommendations to the CI Program and CI Committee.

## Committee Appointees

The CI Committee consists of epidemiologists, environmental specialists, health educators, statisticians, and other specialists who oversee the CI process. Committee representation (required membership) comes from staff members or their designees from DHSS, MCR and MDNR. In addition to the administrators of CHSI, EPH and EPHP, the Chief of BCCDC and the CCCP manager, the following are also appointed members of the committee:

### DHSS Staff

- **Chronic Disease Public Health Epidemiologist** oversees research methodology, supervises case verification and ascertainment and reviews case listings and rate calculations. The **Chronic Disease Public Health Epidemiologist** provides summary and statistical information about cancer cases and serves as state liaison to CDC when that agency's technical services are warranted.
- **Epidemiology Specialist/Research Analyst III** requests, obtains and analyzes case ascertainment and case verification. In addition, this position assists and works in collaboration with the State Epidemiologist to conduct necessary research.
- **BEE staff** provide technical assistance to the CI Program concerning the environmental aspects of cancer inquiries; this may include information on hazardous waste sites and hazardous substances, including dioxin and radiation. This position coordinates with other environmental agencies, including agencies such as the National Institute of Safety and Health (NIOSH), Occupational Safety and Health Administration (OSHA), the federal Agency for Toxic Substances and Disease Registry (ATSDR), Environmental Protection Agency (EPA), and the MDNR. The Environmental Specialist serves as the DHSS liaison with EPA, MDNR, and ATSDR. A significant proportion of cancer inquiries are initially received by environmental health staff and then referred to the CI Program. The Section for

Environmental Public Health designates an environmental specialist to serve as the primary contact for the CI Program.

- **Research Analyst** conducts additional analysis of mortality data used in the cancer inquiry. This position may also provide a listing of people whose cause of death was listed as some form of cancer under investigation to MCR staff for use in case ascertainment. The Bureau of Vital Statistics (BVS) designates a research analyst to serve as the primary contact for the CI Program.
- **CLPHS representative** serves as the CI Program's liaison with LPHAs, as needed. The CLPHS serves as a means for information to travel from the CI Program to the local level and for feedback from the local level to the CI Program.

#### **MCR Staff**

- **MCR representative** (Director and/or Senior Statistician) oversees case verification and may assist with case ascertainment, and serves as liaison with other state cancer registries and the Missouri State Tumor Registrars Association (MoSTRA).

#### **MDNR Staff**

- The **MDNR representative** provides information concerning regulatory issues when immediate environmental health hazards are present. MDNR also assists by providing reports on environmental issues, such as water and air quality. One member of MDNR is designated to be the Department's liaison with the CI Committee in accordance with an inter-agency memorandum of understanding.

The CI Committee may consult with a variety of other organizations or groups to solicit their expertise and input into a CI. Representation may include an individual or individuals from the following organizations and DHSS units:

- **LPHAs** may become involved when an inquiry occurs in their service area and there is significant public concern. These agencies are invited to all open meetings that concern a cancer inquiry issue in their jurisdiction.
- **Public Information Specialist (DHSS)** serves as a consultant for cancer concerns and inquiries. A member of the DHSS OPI team also assists with town hall meetings, press releases, and other communiqués with residents, media groups, etc., surrounding a cancer concern or inquiry.
- **General Counsel (DHSS)** serves as a consultant for cancer concerns and inquiries on an as needed basis.
- A **MoSTRA representative** may provide input into the Committee's review on cancer inquiries and can assist with the process for rapid case ascertainment, as needed, when a Level 2 or Level 3 inquiry is being conducted. The representative shares information with MoSTRA regarding the CI process and linkage, and use of the MCR data.

Technical assistance may also be sought from the OPI, OOE, MCR (Operations Manager, Certified Tumor Registrars), CDC, ATSDR, EPA, and others.

## **Committee Responsibilities**

The CI Committee reviews each report and may recommend changes. The CI Committee conducts reviews of cancer concerns and inquiries, and determines how to proceed. All members receive a summary report the day of the committee meeting outlining the work and research that has been done in response to concerns and inquiries. Committee meetings are held quarterly in accordance with, and subject to, the provisions of the Missouri Open Meeting Law (610.021 Revised Statutes of Missouri), also known as the Sunshine Law. Any discussion of specific cases or any other information that can be linked to an individual's health issues is closed to the public. All DHSS policies are strictly followed concerning the release of information to the public.

Committee members review the report and a vote is taken at the meeting to determine whether to close the concern/inquiry or to recommend it for further investigation. When a concern/inquiry is closed, the CCCP Manager sends a letter and final report to the inquirer. (Refer to Appendix B for a sample report outline.) The report includes all of the information gathered and the findings of the CI Committee. If additional information is needed from the inquirer at this stage, a request for such

information is included in the letter that accompanies the report. If a request is made to an outside agency for help, the CCCP Manager informs the inquirer and explains the next steps.

## Initiation of the Cancer Inquiry Process

The process begins with an initial contact from an individual, a health sector representative, a government agency/official or other entity regarding perceived excess cancer cases or cancer-related deaths in a specific geographical area or sub-population. Contact is usually made by phone, but can be made by letter or email. All incoming messages are referred to the CCCP Manager. The following paragraphs define what is classified as a cancer information request, a cancer concern, and a CI.

### ***Cancer Information Request***

If the initial contact is about a personal cancer concern or the occurrence of excess cancer within the caller's community, it is initially classified as an ***information request***. The CCCP Manager will explore the nature of the cancer concern, provide health education on cancer and lifestyle risk factors, answer questions and send information as requested. The CCCP Manager will record information on the Cancer Inquiry Initial Report Form (Appendix F).

If the discussion and information shared allays the concern and the CCCP Manager (in consultation with CI program staff and possibly internal consultants) sees no indication of a possible cancer cluster, the information request will not be elevated to a cancer concern.

If the discussion reveals that the concern centers on a worksite, the CCCP Manager may refer the inquirer to either the NIOSH or OSHA for investigation.

### ***Cancer Concern***

If the discussion and information shared does not allay the concern and/or CI program staff determines there is a need for more information, the information request may be elevated to a ***cancer concern***.

If the additional information gathered allays the concern, a CI Level 1 inquiry request will not be referred to the CI committee. A concern may also involve issues that are of relevance to other local, state or federal agencies, such as MDNR, EPA, etc.; these will be referred to the appropriate agency.

1. **Cancer Concern – Occupational (Worksite)**: Cancer incidence data submitted to and maintained by MCR includes place of residence at diagnosis, not place of work. Cancer information requests that are referred to NIOSH or OSHA may be identified as a cancer concern after a preliminary investigation by the agency. DHSS may be asked to assist in any research conducted as a result of the referral, and will seek funding for these efforts.
2. **Cancer Concern – Community**: An initial contact may be about a suspected or apparent excess of cancer in a community along with a possible cause. After discussing the information with the CCCP Manager, the individual(s) may better understand cancer and its causes and may not have further concerns about the community. When the inquirer is not satisfied with the information provided, the CI program staff may seek to provide additional information, refer the caller to other agencies or elevate the information request to a cancer concern. At any point, DHSS may take the concern to the CI Committee based on the data and the circumstances.
3. **Requests Related to Previous Inquiries**: If the individual or DHSS is concerned about a geographical area studied in another inquiry, the final public report from that inquiry is either sent to or discussed with the individual, and the inquiry is classified as a concern.

The CCCP Manager will request mortality and incidence data from OOE to determine if the cancer of concern is statistically higher in the area of interest. Data will be extracted only for the specific cancer of concern. The CCCP Manager will work with the epidemiology specialists if the number of cases is statistically higher when compared to the state rate. The CCCP Manager will also coordinate with the epidemiology specialists if additional information is needed to fulfill the inquirer's request. No written report will be generated. Appendix A shows a sample letter that may be sent to an individual with a cancer concern when no follow-up is requested. Appendix F depicts the Cancer Inquiry Initial Report Form with information to be entered into the electronic database when classified as a *cancer concern*.



# Cancer Inquiry Guidelines

The CI process in Missouri is a three-level process. All inquiries begin at Level 1.

## Level 1

### Criteria to move to Level 1 from a concern

Following the initial interview and discussion, the inquirer will be informed (Appendix D) that the facts will be reviewed by the CI Committee to determine what, if any, further action is needed. The Committee then determines whether at least two (2) of the following characteristics are present:

- A. A common type of cancer is occurring in an unexpected age group.
- B. The cancer of interest is rare.
- C. The suspected exposure is plausibly linked to the cancer(s) of concern, based on the available knowledge base and research.
- D. DHSS administration finds that a heightened community concern warrants further action.

If two or more of these characteristics are met, the concern is now moved to a Level 1 inquiry and the initial correspondent is contacted for assistance in distributing patient information forms (Appendix G). The database is updated to reflect this change. All letters, actions, reports, etc., are recorded in the database.

## Level 1 Process

### Phase I

An inquiry is opened, a number is assigned to the inquiry, and records are updated to reflect this new status. This number consists of the year in which the first contact occurs and a number assigned in order (for example, the third inquiry initiated in 2009 would be 09-003.) An in-depth interview is conducted with the initial inquirer or that person's designee. The CI Program staff conducting the interview will discuss health information privacy needs, describe the CI process in detail and inform the initial inquirer about the data collection needs for a Level 1 inquiry, particularly focusing on the Patient Information Form.

Once the initial questions are completed, the remainder of the interview focuses on cancer education; the prevalence of risk factors; screening opportunities for cancer; and the next steps of the inquiry process, if warranted. The information collected during the interview is entered into the Cancer Inquiry database. **Note: Information will be kept confidential in accordance with state and federal laws. At the close of the CI study, patient information forms will be archived according to DHSS confidentiality policies.**

As appropriate, correspondence with inquirers may be copied to appropriate state and local environmental and public health staff. In this correspondence, the name of the inquirer is always kept confidential.

A Level 1 Response Letter (Appendix C) is prepared and sent to the inquirer along with other relevant information, if appropriate, within 10 days. Examples may include:

- *What is Cancer* from the ATSDR,
- *Burden of Cancer in Missouri* (Booklet),
- Mortality and/or incidence rates (if applicable),

#### Resources

- MICA web address (<http://health.mo.gov/data/mica/MICA/>),
- American Cancer Society web address (<http://www.cancer.org/index>),
- Cancer Information Service web address (<http://www.cancer.gov/contact/contact-center>),
- Community Data Profiles (<http://health.mo.gov/data/CommunityDataProfiles/index.html>)
- Surveillance, Epidemiology and End Results Program (<http://seer.cancer.gov/>)
- Any other information specific to the inquiry.

The packet also includes copies of the Cancer Patient Information Form (Appendix G). This form is explained to the inquirer during the phone interview. The inquirer has approximately two (2) weeks to distribute the forms to individuals with cancer and to explain the purpose of the inquiry and use of the forms. The inquirer asks the individuals with cancer to return the forms to DHSS within four (4) weeks. Patients are asked to mail the forms directly to DHSS in order to maintain their confidentiality. DHSS' general legal counsel will be consulted in the event there are questions about the process.

An inquirer who needs more time may contact the CCCP Manager to request additional time. If forms are not received in six (6) weeks, a certified, return-receipt letter (Appendix H) is sent to the

inquirer, explaining that the inquiry will be closed if the CI Program does not hear from the inquirer within two (2) weeks. If the inquirer still does not respond, or if patient forms are not received, the inquiry is considered closed and a certified, return-receipt letter stating such is sent to the inquirer (Appendix I).

## Phase II

Phase II of the Level 1 process begins once the patient information form(s) are returned. The Epidemiology Specialist submits the patient information forms to the MCR. Case verification, a check of the accuracy of information submitted, is conducted by MCR in all cases where the patient information form(s) are received. Cases not confirmed by a medically-reliable source, such as a physician, hospital record or death certificate, are excluded from data analysis. When the case verification is complete, a Level 1 preliminary report is reviewed by the CI Committee to inform their recommendation to DHSS as to whether the inquiry meets the criteria to move it to a Level 2 inquiry.

Case ascertainment, identification of additional cases through active database searches, may also start in Level 1, at the discretion of the State Epidemiologist. CI Program staff, in consultation with the State Epidemiologist and/or the designated epidemiology staff, review the forms and develop a preliminary report (Appendix B). This report is to be submitted to the Committee to determine whether the inquiry meets the criteria to conduct further research and if it should move to a Level 2 inquiry. If it is determined that there is no potential cancer cluster in the community, the inquiry is closed, and a letter is sent to the inquirer informing him or her of this finding and closure.

## Level 2

### Criteria to move to Level 2:

The following conditions should be met in order to consider pursuing a Level 2 inquiry:

- A. At least two of the following Level 1 criteria are met:
  - a. A common type of cancer is occurring in an unexpected age group.
  - b. The cancer of interest is rare.
  - c. The suspected exposure is plausibly linked to the cancer(s) of concern, based on the available knowledge base and research.
  - d. A situation involves heightened community concern and DHSS administration determines such an action is warranted.
- B. Cancer Patient Information Forms have been returned.
- C. A definable type of cancer is reported.
- D. Case verification is completed.
- E. The type or types of cancer being reported has/have a common suspected risk factor(s).
- F. At least one specific environmental or occupational cause (exposure) is suggested for this excess (e.g., dioxin, radiation, asbestos)
- G. A preliminary literature review is conducted and there is no evidence of common behavioral or other risk factors with strong, well-proven relationships to the identified cancer (such as between smoking and lung cancer; between polyvinyl exposure in occupational settings and angiosarcoma; and between asbestos and mesothelioma). There is a plausible scenario for the patients to have come into contact with a suspected cause of the cancer(s). For most cancer sites, if cancer latency is not known, a minimum of ten years' residency in the study area or exposure in the occupational setting is necessary for the suspected association to be considered plausible. Childhood cancers may have a shorter latency period.
- H. If the cancer latency in relation to a particular exposure is known, there is a reasonable match between the estimated time individuals with cancer (cases) were exposed and this latency. If the cluster is in a community setting, the time a case has been exposed is estimated by the time the case lived in the area of concern and the time exposure was first established. If the cluster is in an occupational setting, the time of exposure is estimated by the time the case was employed and when exposure was first established.

If the Cancer Patient Information Forms are not returned and if the inquirer makes no further contact within the designated time frame, there are two (2) circumstances in which the CI Program can still proceed to a Level 2 Inquiry:

- The State Epidemiologist, in collaboration with the CI Committee, concludes that there is enough information to indicate a potential public health risk.
- A situation involves heightened community concern and DHSS administration determines such an action is warranted.

A letter is sent to the inquirer to notify him or her if the inquiry is closed.

## **Level 2 Process**

A Level 2 inquiry involves additional research into specific risk factor(s) for the cancer of concern. Application of epidemiological analytical methods and assessment, including statistical testing, are used to determine if there is an actual cancer cluster. The epidemiological investigation by the Chronic Disease Public Health Epidemiologist and the epidemiology specialist(s) determines if there is a potential cluster of the cancer or cancers of concern. The analytical research conducted includes:

- A. Comprehensive literature search for additional information about risk factors and review of BRFSS and county-level data.
- B. If case ascertainment is not initiated in Level 1, it will be initiated in Level 2. Case ascertainment consists of searching existing databases for cases of the cancer(s) of concern in the geographic location beyond those submitted through the Cancer Patient Information Forms. Case ascertainment may also include requests to reporting facilities to submit basic information on newly-diagnosed cases to MCR prior to completion/before end of 1<sup>st</sup> course of treatment (rapid case ascertainment).
- C. Calculations and statistical testing by geographical area, time periods, and major demographic groups.

A Level 2 preliminary report is prepared and presented to the CI Committee. After reviewing the recommendations and other relevant data and information collected from Levels 1 and 2, the CI Committee determines if there is a potential cancer cluster in the community. If there is not a cancer cluster, the inquiry is closed and a letter is sent notifying the inquirer. The letter is drafted in conjunction with the CI Committee and forwarded to the inquirer and the LPHA through certified mail, and a return receipt is requested.

## **Small Area Analysis**

Small area or zip code level analysis may be conducted in Level 2 inquiries and for special studies. These analyses are conducted due to heightened community concern, when further exploration is warranted due to the impact on the community, the number of cases, or rarity of cancer type with approval from the Chronic Disease Prevention and Nutrition Services Administrator.

## **Level 3**

### **Criteria to move to Level 3**

If clustering of cancer occurrence is supported by the Level 2 research, the following conditions **MUST BE** met before moving to a Level 3 Inquiry:

- A. All conditions and characteristics set forth as criteria for moving to a Level 2 Inquiry are met.
- B. Case ascertainment is initiated and completed.
- C. At least five (5) cases of one type or related types of adult cancer, or at least three (3) cases of one type or related types of childhood cancer per sub-population of interest (age group within gender and race) in the study area.
- D. Statistical calculations indicate the possibility of a cancer cluster. Supportive findings include: statistical results are consistent across tests (congruency among spatial clustering testing and congruency among temporal clustering testing), and are robust to statistical flaws intrinsic in the tests.
- E. There must be an exposed population large enough and well defined enough to conduct a more detailed analytical study with further classification of sub-populations. The Chronic Disease Public Health Epidemiologist oversees research methodology.

If the CI Committee determines there is a possible clustering of cancer occurrence or sufficient evidence, the inquiry moves to Level 3. A letter is sent to the inquirer explaining the reason for proceeding with additional analyses, while providing any other relevant findings. The letter is

drafted in conjunction with the CI Committee and forwarded to the inquirer and the LPHA through certified mail, and a return receipt is requested.

A Level 3 Inquiry **MAY ALSO BE** pursued without the above conditions being met: **IF**:

- In the opinion of the CI Committee, other information or data analysis of the inquiry justify further study of the association between the suspected environmental exposure and the cancer of interest, **OR**
- The CI Committee and DHSS administration find that a heightened community concern is still present surrounding the inquiry.

It should be noted that a Level 3 Inquiry is rare.

### **Level 3 Process**

During a Level 3 inquiry, a more detailed and in-depth epidemiological evaluation is conducted by DHSS and other state and/or federal agencies. The exact research may vary, but may include any or all of the following:

- Literature searches for additional information about risk factors;
- Rapid case ascertainment that encompasses a wider geographical area, additional time periods, and/or searches of other databases;
- Data analysis incorporating either further defined demographic sub-groups, a wider geographical area, or additional time periods;
- Additional statistical testing for assessing consistency in defining the cluster;
- Collection of additional information on the environmental concern, which may include cooperation with other agencies or departments;
- Other information relevant to the specific inquiry.

Once the Level 3 inquiry research and Level 3 preliminary report are completed, data are presented to the CI Committee. The Committee reviews the findings and makes recommendations. Recommendations will vary with the situation, and may range from no further actions are needed to recommending that further studies be conducted. Information on next steps will be shared with the inquirer and other interested parties.

### **Further Studies**

If an environmental assessment concludes that there is an environmental link to the cluster, the environmental epidemiology staff may then be directed to conduct an initial feasibility study and design an analytical study (i.e., epidemiological investigation).

### **Scientific Support for Investigation**

DHSS may request outside agencies, such as CDC and ATSDR, to participate in the feasibility study, environmental exposure assessment, or the design and implementation of the analytical study. This generally occurs when a cancer cluster (excess cancer cases) has been found and the resources needed to conduct further research are beyond the capacity of DHSS.

When an analytical epidemiological study is recommended, it is likely to be conducted by another agency or a research group in an academic setting, with the help of the CI Program and the epidemiology staff. Outside researchers must submit a research plan and receive DHSS' Institutional Review Board approval before confidential data are released.

Once the study is completed a final report is written, approved by the CI Committee, shared with the inquirer and the LPHA, and is posted on DHSS' web site. The report is sent to the inquirer and LPHA through certified mail and a return receipt is requested.

If an analytical study is not feasible, the inquiry is closed and the inquirer is notified. The letter is drafted in conjunction with the CI committee and forwarded to the inquirer and the LPHA through certified mail and a return receipt is requested.

# Analytical Methods

## Epidemiological Evaluation of Cancer Clustering

The evaluation of cancer clusters is not different from other epidemiological evaluations with respect to the use of epidemiological reasoning and principles. These principles are used to guide DHSS staff in every step of the inquiry process to determine if a cancer cluster exists, and if there is a possible cause for that cluster that needs to be examined in an epidemiological investigation. In the same manner of analytical studies, the consistent reliability, biological plausibility (likelihood), and dose-response of the suspected disease and environmental exposure association should be evaluated.

The criteria for deciding whether to initiate additional analytical work at each level of the CI process should address a number of issues: the case and exposure definition (ill-defined or well-defined); length of time (i.e., latency period) between initial exposure and disease diagnosis; plausibility of the exposure pathway; and confounding or other possible explanations for the observed increased incidence and mortality. After conclusion of a Level 3 Inquiry, the feasibility of further epidemiological or environmental investigation is questionable **if** the:

- number of cases is small,
- cancer occurrence is rare,
- environmental exposure is rare,
- cancer occurrence and environmental exposure are both rare, or
- the ability to measure exposure at both the community and the individual level is weak

In addition, the limitations of statistical testing in epidemiological settings are considered. Statistical testing, at its best, can only assist causal reasoning. The “significance” of the epidemiological causality principles and the “significance” of patterns and trends of health events and their implications for public health far outweigh the “significance” of a p-value.<sup>1</sup>

## Study Area

For all levels of a CI, the study area is the smallest identifiable geographical area from which cases arise that allows for reliable rate calculations and statistical testing. The most recent population database (U.S. Census) and annual updated estimates from DHSS are used. The study area is defined by one or more of the following: county, ZIP, census tract, Metropolitan Statistical Area (MSA), or city.

Other possible study areas include schools and occupational settings for which both the total number of cases and the total population size can be reported and later verified and ascertained. Typically, areas larger than, and contiguous to, the study area should be used as a comparison during a cancer cluster investigation. It is possible that after case verification (Level 1 Inquiry) and case ascertainment (Level 2 Inquiry), the boundaries of the study area may be modified.

## Study Period

The study period usually corresponds to the identified dates of incident or deceased cases reported on the CI Inquiry Program Response and Cancer Patient Information Forms for Level 2 and above inquiries. For a Level 3 Inquiry, the study period may correspond to verified and ascertained incident or deceased cases.

In an inquiry situation where an insufficient number of cases are identified but an inquiry is perceived as necessary, DHSS administration and the CI Committee, in consultation with the State Epidemiologist, may decide to pursue further research. In this situation, additional years of incidence and mortality data, if available, are used beyond the years indicated by the CI Initial Report Form and the Cancer Patient Information Form.

In a situation when the evaluation of evidence for clustering at Level 2, Level 3, or Level 4 is not statistically significant, but there is plausibility for establishing a cluster, additional years of data may be used to increase the statistical power of the analysis.

## Population

A choice of study (population at risk or index population) and comparison populations for statistical calculations, including area and period, as well as sub-populations (gender, race and age groups), will be dictated by the availability of population-based data.

Population-based data used for rate calculation may include the most current U.S. Census, the most current Missouri Census, or updated U.S. or Missouri inter-census population estimates by gender, race and age group that are provided by the National Center for Health Statistics (NCHS) and DHSS's BHI, respectively. For standard U.S. and Missouri comparison incidence rates, population-based incidence rates are the SEER Program, the NAACCR, the U.S. Cancer Statistics, or the MCR, respectively. The source depends upon the time period involved.

Ideally, at a Level 2 Inquiry, sub-population analysis should include classification of cancer occurrence and death by gender and race, regardless of the choice of study area and period. At Level 3 inquiries, further classification of rates into age-specific groups is warranted as is classification by occupation and smoking status if data are available. Childhood cancers are the exception to this classification of sub-populations. Also, because index (study) population observed rates and counts are compared to rates expected from a comparison population, the choice of the study population is made in conjunction with identification of a comparable population.

## Cancer Sites

Only primary tumor sites are studied. For example, if the inquiry is focused on possible excess brain cancer, cases will be included only if the brain is the primary site. Cases where the cancer has metastasized (i.e., spread) to the brain from a different primary site (e.g., lung, breast, etc.) will be excluded from analyses. Primary sites are identified using ICD-O-3 codes for incidence cases and ICD-10 codes for cases identified through death files.

For initiation of Level 2 Inquiry calculations, it may be assumed that the case notification by the individual and others submitting Cancer Patient Information Forms is adequate. Whenever possible, calculations are made using both this information and any additional cases verified by MCR in the study area. For Level 3 Inquiries, thorough case ascertainment of diagnosis will determine accuracy of reported sites.

If the individual's report involves more than one site, attempts will be made to calculate incidence and mortality statistics for all sites involved during a Level 2 or Level 3 Inquiry. If only one cancer site is involved, then incidence and mortality statistics are calculated for this site and for "all cancer" by the same sub-populations as described under the population section. If the inquiry concerns a childhood cancer, the SEER pediatric major cancer group that includes the cancer of interest, will be used instead.<sup>8</sup>

## Case Verification and Case Ascertainment

### Case Verification

For a Level 2 Inquiry, the information from the inquirer and the Cancer Patient Information Form(s) is verified for accuracy of diagnosis (site, histology and stage), date of diagnosis, address of patient or decedent at time of diagnosis, demographic factors (sex, race, date of birth, marital status, occupation, etc.), and risk factors (smoking history and toxic exposure, if available). Primary verification sources include the MCR database, as well as mortality data and possibly other sources such as hospital discharge data, specific program data and records from physician offices, clinics, path labs, etc.

### Case Ascertainment

Case ascertainment may be initiated in Level 1 or Level 2. Rapid case ascertainment may be needed to obtain information on recently diagnosed cases in Level 3. Usually it is conducted if the Chronic Disease Public Health Epidemiologist and/or the CI Committee make the recommendation. Case ascertainment involves an active search for additional cases in the study area by CI staff and MCR staff. It also includes double-checking for inconsistencies in: primary site, date of diagnosis, date of death (if applicable), and additional verification of address, demographics, time residing in the

study area, occupational activities, and geocoding for precise determination of the geopolitical study area.

## Methods for Detecting Space & Time Clustering

Whenever possible, calculation of standardized rates and ratios will be the methods of choice to determine space and time clustering of cancer cases.

At both Level 2 and Level 3 Inquiries, whenever data are appropriate, incidence and mortality rates and the corresponding 95% confidence intervals will be calculated for the study population (as defined by study area and period of time). Direct or indirect methods for adjustment to different age distributions between comparison populations will be used.<sup>2, 3, 5</sup>

The standardized incidence and mortality ratios of the index (study) population by the comparison population (such as SEER or NAACCR-U.S. or MCR-Missouri) and the 95% confidence interval are used to evaluate space and time clustering when the number of cases and denominator are sufficient to generate reliable rate and ratio estimates.

## Limitations of Methods

Many (more than expected) occurrences of cancer clusters are observed when cancer cases are distributed in an ever-increasing number of arbitrarily defined study areas. In the words of Bender “if an area is examined in detail for a long period of time, a statistically significant excess of cancer cases will be observed.”<sup>4</sup> Clusters are not rare occurrences. With over 300 million people in the United States and many types of cancer, chance alone may explain many identified clusters. Clusters occur continually within any large population, and their population occurrence is often no greater than that expected by chance alone. Therefore, cancer clusters often represent “expectedly unexpected events.”<sup>9</sup>

The manner by which cancers are detected can affect rate comparisons. Screening and early diagnosis capabilities may change over time and by region. The rate comparisons and the statistical testing utilized assume this bias is not operating. Therefore, these variations may result in differences when comparing rates and counts by time periods and regions.<sup>4</sup>

Screening and diagnostic technique changes that are different across regions, and time periods can affect cancer staging. Cancer that has metastasized at some point in time may have been misclassified as localized or regionalized cancer at an earlier date due to this bias.<sup>10</sup>

## Epidemiological Translation

Application of epidemiological criteria for disease causation and reasoning should guide the CI process. Statistical tools are used to assist in making a decision about the existence of a cluster, never to determine this decision.

The criteria for causality of an association that guides the epidemiologist, and therefore the CI process, are the consistency, biologic plausibility and evidence of dose-response.

The consistency criterion requires a wide knowledge base of the natural history and descriptive epidemiology of the reported cancer(s) as well as the use of a systematic literature review that incorporates the principles of evidence-based research. In terms of cluster investigation, consistency may mean any of the following:<sup>7</sup>

- Historical patterns in the reported cases;
- Pattern(s) of occurrence consistent across reported literature;
- Homogeneity of reported cases (e.g., same sex, race, age or occupation; same cell type, anatomic site or pathway of exposure); and/or
- Consistency within aggregation (within cluster).

Biologic plausibility requires a strong knowledge of the disease process of concern and reliable information on environmental exposure of interest. In the context of a CI, the biologic plausibility may mean any of the following:

- Presence of an environmental or occupational risk (e.g., asbestos abatement and mesothelioma);
- Demonstration that a pathway for exposure is possible; and/or
- Recognition that a specific organ or tissue is a possible site for biologic action of the suspected exposure.

In analytical epidemiology and medical research, dose-response is considered by far one of the strongest criteria for determining a causal association. However, cluster investigations are hypothesis-generating types of research, as opposed to analytical studies that are designed to test hypotheses of causation. This difference is carried over to the careful application of criteria and the interpretation of the findings of a cluster investigation. Often the dose-response is evaluated against the time continuum. For this reason, a series of reported cases over a long period of time is usually required to assess this criterion in a meaningful way. Sometimes dispersion of spatial patterns may also be used to assess dose-response.

In a cluster investigation, dose-response usually means:

- Duration of exposure (e.g., a greater proportion of cases with long-term residency in the proximity of the hazard or proximity in time of suspected events).

In a cluster investigation, dose-response less often means:

- Identification of a specific spatial pattern of dispersion (e.g., the closer the proximity to the exposure, the greater the number of observed cases); or,
- A combination of duration of exposure and spatial pattern of dispersion.



# APPENDIX A

## Sample Letter of Concern Response

*SEND CERTIFIED MAIL, RETURN RECEIPT REQUESTED  
VERIFY WEBLINKS BEFORE SENDING*

[Date]

CI<00-000>

[Name]

[Address]

[City, state, zip code]

Dear [Insert name]:

Thank you for sharing your concerns about possible excess <specific> cancer in <region name> that you think is linked to <suspected cause>. The number of cases and the death rate of <specific> cancer in <region name> are <higher than/lower than/similar to> the state. <Include BRFSS or screening statements if appropriate, such as: Smoking rates are also higher than the state. >

Cancer is very serious and scary to many, but it is in fact very common. About one in three Americans will develop cancer in their lifetimes, and will affect three out of four families. The chance of having cancer also increases with age, so as our population gets older, we will see more cancer cases.

Cancer is not one disease, but many. It can occur in almost any part of the body. Each cancer develops differently and has different risk factors. For example, the main risk factor for lung cancer is cigarette smoking and it is sun exposure for skin cancer. However, there are many factors related to breast cancer, some of which are known and some which are not known.

Many believe that something in the area they live causes cancer. In truth, personal habits like tobacco use, poor diet, excessive sun exposure and alcohol use are much more likely to contribute to cancer. Exposure to things in the environment cause less than 10% of cancers, while cigarette smoking alone causes about 30% of cancers. Family and medical histories and some communicable diseases, such as the human papilloma virus or HPV (cervical cancer), hepatitis (liver cancer) or helicobacter pylori (stomach cancer) can also increase the likelihood of some types of cancer.

Most cancers take a long time to develop. Some may take as many as 40 years. This is one of the reasons that cancer is more common in older adults. A few chemicals are known to cause some certain types of cancer, but a person must be in contact with these chemicals for a long period of time before cancer develops.

A cancer cluster is more cases of cancer than normal in an area over a period of time. A cluster is made up of only one type of cancer, most of the time. When the kinds of cancer vary, such as lung, breast, leukemia, and prostate, it usually is not a "true" cluster. For this reason, a study of people with different cancer types will not shed light on the cause. That is why it is important to have details about the people and the cancer that seem to be part of a cluster. A "true" cancer cluster usually involves one or more of the following:

- Only one type of cancer;
- Cancer in an unexpected age group;
- A very rare type of cancer; or
- Science has established that the suspected exposure may cause the cancer of concern.

You may also look at our sources for cancer data for Missouri and your county. The Missouri Information for Community Assessment (MICA) was set up for the public, and is easy to use. The web address is <http://health.mo.gov/data/mica/MICA/>

Several health agencies and other health officials will get a copy of this letter. This is so they will know about the concern. Your name and address will not be included on those copies. This is to protect your privacy. If you have questions, please call <name of contact person> at 573 522-2841.

Sincerely,

<name>

Cancer Inquiry Coordinator

<AA> : <bb>

Enclosures

- c: <name>, Administrator, Section for Community Health Services and Initiatives
- <name>, Administrator, Section for Epidemiology for Public Health Practices
- <name>, Administrator, Section for Environmental Public Health
- <name>, Chief, Bureau of Cancer and Chronic Disease Control
- <name>, Director, Center for Local Public Health Services
- <name>, Chief, Bureau of Environmental Epidemiology
- <name>, Chronic Disease Public Health Epidemiologist, Office of Epidemiology
- <name>, Chief, Office of Public Information
- <name>, Administrator, <name> Local Public Health Agency

# Appendix B

## Report Outline

CI No:

Location:

Received:

Initiator:

Type(s) of cancer reported:

Suspected Cause(s):

Summary of inquiry:

Data:

Patient Information:

Criteria

Because the criteria change with each level of progression, the report should include whatever criteria were used to determine if the CI should move to the next level (see Level 1, Level 2 and Level 3 Guidelines for criteria).

# Appendix C

## Sample Level 1 Response Letter

*VERIFY WEBLINKS BEFORE SENDING*

Date

CI<00-000>

Name

Address

City, state, zip code

Dear [Insert name]:

Thank you for sharing your concerns about possible excess <specific> cancer in <region name> that you think is linked to <suspected cause>. The number of cases and the death rate of <specific> cancer in <region name> are <higher than/lower than/similar to> the state. <Include BRFSS or screening statements if appropriate, such as: Smoking rates are also higher than the state. > The Missouri Department of Health and Senior Services (DHSS) forwarded this information to the Cancer Inquiry Committee to consider for opening a cancer inquiry, and they have requested additional information to make further determinations.

The first step in starting the cancer inquiry is to distribute the enclosed Patient Information forms to those individuals with cancer in your community of concern. Explain to them that this information is necessary to assist the Missouri Department of Health and Senior Services in investigating your concern. Additional information in this letter can assist you in educating them. Due to confidentiality requirements, each individual needs to return his or her own form to Department of Health and Senior Services, Bureau of Cancer and Chronic Disease Control, Cancer Inquiry Program, PO Box 570, Jefferson City, MO 65102-0570. (The address is printed on the form.) **It is important that these forms are returned.** Each person should provide the best information available.

Please ask each individual to return the enclosed forms within six (6) weeks. It is important that you follow-up with them to find out if the forms have been sent. If we do not receive any forms within six weeks, our office will assume that no further action is necessary and will close the inquiry. If more than six weeks is needed to get all of the forms to us, please contact <name> in our office at (573) 522-2841.

Enclosed are several items with more information about cancer and Missouri's formal cancer inquiry process: <include list of what was enclosed> Additional information can be obtained at these websites:

- "The Burden of Cancer in Missouri":  
<http://health.mo.gov/living/healthcondiseases/chronic/chronicdisease/cancerburdenreport.pdf>
- Cancer Inquiry website: <http://health.mo.gov/living/healthcondiseases/chronic/cancerinquiry/index.php>

The DHSS website can also provide valuable cancer incidence data via MICA the Missouri Information for Community Assessment (MICA). The general public, as well as researchers, local public health agencies, and others can access cancer data on MICA at <http://health.mo.gov/data/mica/MICA/>.

For any other questions, please call 573 522-2841.

Sincerely,

Cancer Inquiry Coordinator

Enclosures

c: <name>, Administrator, Section for Community Health Services and Initiatives  
<name>, Administrator, Section for Epidemiology for Public Health Practices  
<name>, Administrator, Section for Environmental Public Health  
<name>, Chief, Bureau of Cancer and Chronic Disease Control  
<name>, Director, Center for Local Public Health Services  
<name>, Chief, Bureau of Environmental Epidemiology  
<name>, Chronic Disease Public Health Epidemiologist, OOE  
<name>, Chief, Office of Public Information  
<name>, Administrator, <name> Local Public Health Agency

# APPENDIX D

## Sample Further Review Letter

*SEND CERTIFIED MAIL, RETURN RECEIPT REQUESTED  
VERIFY WEBLINKS BEFORE SENDING*

Date

CI<00-000>

Name

Address

City, state, zip code

Dear [Insert name]:

Thank you for sharing your concerns about possible excess <specific> cancer in <region name> that you think is linked to <suspected cause>. The number of cases and the death rate of <specific> cancer in <region name> are <higher than/lower than/similar to> the state. <Include BRFSS or screening statements if appropriate, such as: Smoking rates are also higher than the state. > The Missouri Department of Health and Senior Services (DHSS) has forwarded this information to the Cancer Inquiry Committee to consider for opening a cancer inquiry. Should the criteria for opening an inquiry be met for the possible excess cancer you have reported, we will contact you to discuss further steps.

Cancer is very serious and scary to many, but it is in fact very common. About one in three Americans will develop cancer in their lifetimes, and will affect three out of four families. The chance of having cancer also increases with age, so as our population gets older, we will see more cancer cases.

Cancer is not one disease, but many. It can occur in almost any part of the body. Each cancer develops differently and has different risk factors. For example, the main risk factor for lung cancer is cigarette smoking and it is sun exposure for skin cancer. However, there are many factors related to breast cancer, some of which are known and some which are not known.

Many believe that something in the area they live causes cancer. In truth, personal habits like tobacco use, poor diet, excessive sun exposure and alcohol use are much more likely to contribute to cancer. Exposure to things in the environment causes less than 10% of cancers, while cigarette smoking alone causes about 30% of cancers. Family and medical histories and some communicable diseases, such as the human papilloma virus or HPV (cervical cancer), hepatitis (liver cancer) or helicobacter pylori (stomach cancer) can also increase the likelihood of some types of cancer.

Most cancers take a long time to develop. Some may take as many as 40 years. This is one of the reasons that cancer is more common in older adults. A few chemicals are known to cause some certain types of cancer, but a person must be in contact with these chemicals for a long period of time before cancer develops.

A cancer cluster is more cases of cancer than normal in an area over a period of time. A cluster is made up of only one type of cancer, most of the time. When the kinds of cancer vary, such as lung, breast, leukemia, and prostate, it usually is not a "true" cluster. For this reason, a study of people with different cancer types will not shed light on the cause. That is why it is important to have details about the people and the cancer that seem to be part of a cluster. A "true" cancer cluster usually involves one or more of the following:

- Only one type of cancer;
- Cancer in an unexpected age group;
- A very rare type of cancer; or
- Science has established that the suspected exposure may cause the cancer of concern.

You may also look at our sources for cancer data for Missouri and your county. The Missouri Information for Community Assessment (MICA) was set up for the public, and is easy to use. The web address is <http://health.mo.gov/data/mica/MICA/>.

Several health agencies and other health officials will get a copy of this letter. This is so they will know about the concern. Your name and address will not be included on those copies. This is to protect your privacy. If you have questions, please call 573 522-2841.

Sincerely,

<name>

Cancer Inquiry Coordinator

<AA> : <bb>

Enclosures

- c: <name>, Administrator, Section for Community Health Services and Initiatives
- <name>, Administrator, Section for Epidemiology for Public Health Practices
- <name>, Administrator, Section for Environmental Public Health
- <name>, Chief, Bureau of Cancer and Chronic Disease Control
- <name>, Director, Center for Local Public Health Services
- <name>, Chief, Bureau of Environmental Epidemiology
- <name>, Chronic Disease Public Health Epidemiologist, OOE
- <name>, Chief, Office of Public Information
- <name>, Administrator, <name> Local Public Health Agency

# Appendix E

## Does Not Meet Inquiry Criteria Letter

Date

CI<00-000>

Name

Address

City, state, zip code

Dear [Insert name]:

Thank you for sharing your concerns about possible excess <specific> cancer in <region name> that you think is linked to <suspected cause>. According to the Cancer Inquiry Protocol, the initial review of cancer and risk factor data typically begins at the county level and then, if the findings support, moves to smaller area analysis. The Missouri Department of Health and Senior Services (DHSS), Office of Epidemiology has reviewed the cancer and risk factor data for <place> from the Missouri Cancer Registry, the Missouri Information for Community Assessment (MICA), and the 2007 Missouri County-level Study. In addition, the submitted patient information forms were reviewed and case verification completed by Missouri Cancer Registry (MCR).

Analyses of the cancer data were completed to make a cancer excess determination for your area. Attached is the full report that details the findings of the analysis. Below is a summary of the report.

**Include excerpts from the findings....**

The Cancer Inquiry Committee recommends that this Cancer Inquiry be closed for the following reasons:

**List reasons for not meeting criteria**

If you have any additional questions regarding this analysis or the findings and recommendations, please do not hesitate to call the Cancer Control Program at 573-522-2841.

Sincerely,

<name>

Cancer Inquiry Coordinator

<AA> : <bb>

Enclosures

c: <name>, Administrator, Section for Community Health Services and Initiatives  
<name>, Administrator, Section for Epidemiology for Public Health Practices  
<name>, Administrator, Section for Environmental Public Health  
<name>, Chief, Bureau of Cancer and Chronic Disease Control  
<name>, Director, Center for Local Public Health Services  
<name>, Chief, Bureau of Environmental Epidemiology  
<name>, Chronic Disease Public Health Epidemiologist, OOE  
<name>, Chief, Office of Public Information  
<name>, Administrator, <name> Local Public Health Agency

# Appendix F

## Cancer Inquiry Initial Report Form

Date:	DHSS Employee Completing Form:		
<b>Caller Information:</b>			
Name:			
Address:			
City/State/Zip:			
Phone #:		Best Time to Contact:	
E-Mail Address:			
<b>Concern Information:</b>			
City:		County:	Zip Code:
Geographical Boundaries:			
Suspected Exposure (provide information on what the caller suspects caused the cancers – chemicals on the job, factory emissions, seepage from landfill, etc...)			
<b>Type(s) of Cancer(s) of Concern:</b>			
Time period of Diagnoses (e.g. 1989-1994)	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> to <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Time period of Exposure (e.g. 1965-2001)	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> to <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
		Is exposure still occurring? <input type="checkbox"/> Yes <input type="checkbox"/> No	
Have other government agency been contacted about this possible exposure? <input type="checkbox"/> Yes <input type="checkbox"/> No			
<b>Public Officials Contacted</b>			
Name:		Title:	
Agency:			
Address:			
City/State/Zip:			
Phone Number(s):			
E-Mail Address:			
<b>Summary of Conversation (Date   Notes) (Use back of form if necessary)</b>			



# Appendix G

## Patient Information Form

*VERIFY WEBLINKS BEFORE SENDING*

**Purpose of Patient Information Form:** For individuals within the community to report cancer or benign brain/central nervous system (CNS) tumors.

Cancer is a general name for more than 100 different diseases, all of which are characterized by uncontrolled growth and spread of abnormal cells. Cancer can arise in many different sites, behave differently depending on its site of origin and have a variety of causes. The complex nature of cancer makes it very difficult to identify, interpret and address a perceived excess of cancer. The time between exposure to a cancer-causing agent, or the existence of other risk factors, and the development of cancer can be decades; therefore, causes are hard, and sometimes impossible, to identify. A suspected excess of cancer is more likely to be a true cluster, rather than a coincidence or chance occurrence, if it involves one or more of the following:

- A large number of one type of cancer, rather than several different types.
- A rare type of cancer, rather than common types.
- An increased number of cases of a certain type of cancer in an age group that is not usually affected by that type of cancer.

Confirmation of a cancer excess in a community does not necessarily mean that there is any single, external cause or hazard that can be identified. A confirmed excess of cancer could be the result of any of the following:

- Chance;
- Miscalculation of the expected number of cancer cases (e.g., not considering a risk factor within the population at risk);
- Differences in the case definition between observed cases and expected cases;
- Genetic causes
- A known, non-environmental cause (e.g., smoking, alcohol consumption); or
- An unknown cause (e.g., several cases of the same cancer type in a family may be linked to inherited gene changes which increase the chance of developing cancer).

In Missouri, the Missouri Department of Health and Senior Services (DHSS) usually provides the first response to a suspected excess of cancer, following steps outlined in DHSS's *Cancer Inquiry Protocol* (see below). Completion of the Patient Information Form is the first step in responding to an inquiry about possible excess cancer or benign brain/CNS tumors in your community. **Please fill in all of the information requested on the Patient Information Form as completely as possible. The information you provide, whether for yourself or a family member, will be kept confidential according to state and federal laws and guidelines.** DHSS uses this information to confirm that the case has been reported by the medical community to the Missouri Cancer Registry, as required by law, and also to determine whether there is a greater-than-expected number of cases of a particular cancer in the community.

**Further information about cancer, tumors, perceived excess of cancer and the cancer inquiry process can be found at the following websites or by calling (573) 522-2841:**

- Missouri Department of Health and Senior Services: <http://health.mo.gov/living/healthcondiseases/chronic/cancerinquiry/index.php>
- Centers for Disease Control and Prevention: [www.cdc.gov/nceh/clusters/default.htm](http://www.cdc.gov/nceh/clusters/default.htm)

- National Institutes of Health <http://health.nih.gov/topic/CancerGeneral>
- Missouri Information for Community Assessment (MICA): <http://health.mo.gov/data/mica/MICA/>

## **Risk Factors for Developing Cancer**

Doctors often cannot explain why one person develops cancer and another does not. But research shows that certain “risk factors” increase the chance that a person will develop cancer. These are the most common risk factors for cancer:

- Growing older
- Tobacco exposure
- Sunlight -- ultraviolet (UV) radiation that comes from the sun, sunlamps and tanning booths
- Ionizing radiation -- radioactive fallout, radon gas, X rays and other sources
- Exposure to certain chemicals and other substances, such as asbestos, benzene, cadmium, or vinyl chloride (most likely in the workplace)
- Some viruses and bacteria – human papilloma viruses, hepatitis B or C, human immunodeficiency virus or HIV, Helicobacter pylori, etc.
- Certain hormones
- Family history of cancer
- Alcohol consumption
- Unhealthy diet, lack of physical activity, or being overweight

Some risk factors, such as family history, cannot be avoided. However, many cancer risk factors can be avoided. People can help protect themselves by staying away from known risk factors whenever possible. If you would like information on any cancer topics, please visit the website at <http://www.dhss.mo.gov> or call (573) 522-2841.

**If you think you may be at increased risk for cancer, you should discuss this concern with your doctor. You may want to ask about how to reduce your risks and about a schedule for checkups.**



**MISSOURI DEPARTMENT OF HEALTH AND SENIOR SERVICES  
 PATIENT INFORMATION FORM  
 TO REPORT CANCER OR BENIGN BRAIN/CNS TUMORS**

CI _____ - _____ - _____ PIF _____ (For agency use)
---

Patient information will be kept confidential according to state and federal laws and guidelines.

<b>*Legal Name</b> <small>(at time of diagnosis)</small>			_____	_____	_____
	Last Name	First Name	Middle Name or Initial		
Current Street or Mailing Address _____					
City / State / Zip _____					
Phone Number (_____) _____ - _____			* Gender <input type="checkbox"/> Male <input type="checkbox"/> Female		
*Social Security Number _____ - _____ - _____			*Birth Date ____/____/____		
*Type of cancer or tumor			Occupation (at time of or prior to diagnosis)		
*Month/Year of diagnosis			Date of death ( if deceased)		
*Address at time of diagnosis <small>(street address, city, county, state, and zip)</small>					# Years at this address
Physician's name <small>(who made diagnosis)</small>			Facility where cancer diagnosis was made (Hospital or other facility)		
After reviewing the risk factors, what do you think may have caused this cancer or benign tumor?					
Additional Information & Comments: Please provide any additional information that you think would be useful on the back of this page or attach a separate sheet of paper.					
Is patient aware his/her name is being reported? <input type="checkbox"/> <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> NA, patient deceased					
Name, contact information, and relationship of person completing this form if not the same as patient.					
<b>Please return this form to:</b> Bureau of Cancer and Chronic Disease Control Cancer Inquiry Program Missouri Department of Health & Senior Services P. O. Box 570, Jefferson City MO 65102-0570					
<b>For MCR use only</b> <u>Fields verified:</u> (verify on PIF & enter if different)			In Database: _____ Yes _____ No <u>Additional information:</u> (from MCR database)		
SS# _____			Site: _____ HIST/BEHV/GRD _____		
DOB _____			Stage: _____		
Address @ dx _____			Other: _____		
Date of dx _____					

# Appendix H

## Sample Patient Information Forms Returned Letter

*SEND CERTIFIED MAIL, RETURN RECEIPT REQUESTED  
VERIFY WEBLINKS BEFORE SENDING*

[Date]

CI<00-000>

[Name]

[Address]

[City, state, zip code]

Dear Insert name]:

A letter and Cancer Patient Information Forms were sent on <date> requesting your assistance in researching your concerns about an excess of cancer cases in your community. Upon review, our files indicate that no forms have been received, and we have not been contacted for a time extension. These forms are necessary to proceed with the inquiry.

Because no further research into your concerns can be done without the Cancer Patient Information Forms, the CI Program will consider this inquiry closed if our office does not receive a response within two (2) weeks of the date of this letter. If additional time is needed for individuals to send us the Cancer Patient Information Forms, simply notify this office and we can provide up to an additional four (4) weeks.

As with our previous letter, your name and address have been omitted from the copies being sent to other offices to maintain your confidentiality. The copies serve to inform those offices of the status of the cancer concern in the community.

Additional cancer information can be obtained at these websites:

- “The Burden of Cancer in Missouri”:  
<http://health.mo.gov/living/healthcondiseases/chronic/chronicdisease/cancerburdenreport.pdf>
- Cancer Inquiry website: <http://health.mo.gov/living/healthcondiseases/chronic/cancerinquiry/index.php>

If you have any questions, please call 573-522-2841.

Sincerely,

<Name>

Cancer Inquiry Coordinator

VW:ta

- c: <name>, Administrator, Section for Community Health Services and Initiatives  
<name>, Administrator, Section for Epidemiology for Public Health Practices  
<name>, Administrator, Section for Environmental Public Health  
<name>, Chief, Bureau of Cancer and Chronic Disease Control  
<name>, Director, Center for Local Public Health Services  
<name>, Chief, Bureau of Environmental Epidemiology  
<name>, Chronic Disease Public Health Epidemiologist, OOE  
<name>, Chief, Office of Public Information  
<name>, Administrator, <name> Local Public Health Agency

# Appendix I

## Final No Patient Information Forms Returned Letter

*SEND: CERTIFIED MAIL, RETURN RECEIPT REQUESTED  
VERIFY WEBLINKS BEFORE SENDING*

Date

CI<00-000>

Name

Address

City, state, zip code

Dear [Insert name]:

A letter and Cancer Patient Information Forms were sent on <DATE>, and a follow-up letter was sent on <DATE>, requesting your assistance in researching your concerns about an excess of cancer cases in your community. Upon review, our files indicate that no forms have been received, nor have we been contacted for a time extension.

Because no further research into your concern can be completed without this information, the inquiry is now closed. Your name and address have been omitted from the copies of this letter being provided to other offices to maintain your confidentiality. The copies serve to inform those offices of the nature of and status of the cancer concern in the community. Additional cancer information can be obtained at these websites:

- “The Burden of Cancer in Missouri”:  
<http://health.mo.gov/living/healthcondiseases/chronic/chronicdisease/cancerburdenreport.pdf>
- Cancer Inquiry website: <http://health.mo.gov/living/healthcondiseases/chronic/cancerinquiry/index.php>

If you have any questions, please call 573-522-2841.

Sincerely,

<NAME>

Cancer Inquiry Coordinator

VW:ta

- c: <name>, Administrator, Section for Community Health Services and Initiatives  
<name>, Administrator, Section for Epidemiology for Public Health Practices  
<name>, Administrator, Section for Environmental Public Health  
<name>, Chief, Bureau of Cancer and Chronic Disease Control  
<name>, Director, Center for Local Public Health Services  
<name>, Chief, Bureau of Environmental Epidemiology  
<name>, Chronic Disease Public Health Epidemiologist, OOE  
<name>, Chief, Office of Public Information  
<name>, Administrator, <name> Local Public Health Agency

# Appendix J

## Sample Confirmation Letter

*SEND CERTIFIED MAIL, RETURN RECEIPT REQUESTED*

CI<00-000>

DATE

NAME  
ADDRESS  
CITY, STATE, ZIP

Dear [Insert name]:

This letter is to confirm that the Missouri Department of Health and Senior Services, Cancer Inquiry Program has received Cancer Patient Information Forms. Thank you for facilitating the return of these forms.

The next step in the Cancer Inquiry process is to verify the information on the Cancer Patient Information Forms with Missouri Cancer Registry records. The information is then compared against a set of criteria to determine if further research is required. This may take between a few weeks to a few months to complete. Your patience during this time is appreciated. The Cancer Inquiry staff will communicate the results to you as soon as possible.

This inquiry will be discussed at the next Cancer Inquiry committee meeting scheduled for <date>. If it is determined that there is no clustering of cancer cases in your community and the identified environmental exposure does not represent a community health hazard, a letter describing the findings will be forwarded within <number> weeks after the Cancer Inquiry committee meeting. However, if it is determined that there is a possible cancer cluster, further research and evaluation may take an additional two to three months to complete. After this evaluation is complete, the Cancer Inquiry staff will provide a detailed description of the findings.

Please contact the Cancer Inquiry staff at (573) 522-2841 to provide any new information that may be helpful or to ask questions.

Sincerely,

<name>  
Cancer Inquiry Coordinator

VW:ta

c: <name>, Administrator, Section for Community Health Services and Initiatives  
<name>, Administrator, Section for Epidemiology for Public Health Practices  
<name>, Administrator, Section for Environmental Public Health  
<name>, Chief, Bureau of Cancer and Chronic Disease Control  
<name>, Director, Center for Local Public Health Services  
<name>, Chief, Bureau of Environmental Epidemiology  
<name>, Chronic Disease Public Health Epidemiologist, OOE  
<name>, Chief, Office of Public Information  
<name>, Administrator, <name> Local Public Health Agency

# Definitions

- Age-adjusted Rate.....A procedure for adjusting rates, designed to minimize the distortions created by differences in age distributions (and permit fair comparisons) when comparing rates for populations with different age compositions. This calculation is useful when comparing rates from different populations or in the same population over time. Age-adjusted rates are calculated by weighting the age-specific rates for a given year by the age distribution of a standard population. Source: Commonwealth of Massachusetts Department of Public Health. *Heart disease and cancer*. Retrieved February 16, 2006, from <http://www.mass.gov/dph/bhsre/death/96/dth96app.htm>)
- Age-specific Rate .....Age-specific rates are computed by dividing the number of events (e.g. deaths) in an age group in an area by the estimated population of the same age group/area and then multiplying by 100,000 or the appropriate multiplier. Age-specific rates are used in computing age-adjusted rates. Based on: Anderson RN, Rosenberg HM. Age Standardization of Death Rates: Implementation of the Year 2000 Standard. Source: National vital statistics reports; vol 47 no. 3. Hyattsville, Maryland: National Center for Health Statistics. 1998, found at: [http://www.cdc.gov/nchs/data/nvsr/nvsr47/nvs47\\_03.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr47/nvs47_03.pdf)
- Case Analytical Study .....The testing of hypotheses (i.e., testable assumptions) to determine if the differences between two or more variables are independently occurring.
- Case Ascertainment.....The process of identifying new cases through an active search of existing cancer databases.
- Case Verification .....The process of verifying the accuracy of information on each case submitted. The MCR database is the usual data source for case verification.
- Cancer Incidence Rate .....Incidence rates express the number of **new** cases diagnosed in a population with respect to the size of the population and the time period under study. Source: Havener L (Ed). Standards for Cancer Registries Volume III: Standards for Completeness, Quality, Analysis, and Management of Data. Springfield (IL): North American Association of Central Cancer Registries. October 2004.)
- The frequency (number) of new occurrences (cases) of cancer reported in a specified period of time (e.g., a year) divided by the number of persons in the population (e.g., county, region, state, etc.) during the time period being studied. Source: Brownson, R.C., Remington, P.L., & Davis, J.R. (1998). *Chronic disease epidemiology and control* (2<sup>nd</sup> ed.). Washington, DC: American Public Health Association.
- Cancer Cluster .....A greater-than-expected number of cancer cases that occurs within a group of people in a defined geographic area over a specific period of time.
- Confidence Interval (CI).....A confidence interval (CI) is a range around a measurement, such as a rate, which shows the precision of the measurement. The CI indicates the probability that the measurement will fall between the upper and lower limits of the interval a given percentage of the time. For example, a 95% CI will include the true value of the measurement 95% of the time.
- Crude Rate .....A rate is a measure of some event, disease, or condition in relation to a unit of population, along with some specification of time. For example,

a crude death rate is calculated by dividing the number of deaths in a population in a year by the number of persons in that population. The term "crude" distinguishes rates calculated as just described from rates that are adjusted for some characteristic, such as age. [See Age-adjusted rate.] Death rates are expressed as the number of deaths per 100,000 population; rates for other events or conditions may use other multipliers. Source: Adapted from "NCHS Definitions" at <http://www.cdc.gov/nchs/dataawh/nchsdefs/rates.htm#crudedead>

- Death (Mortality) Rate .....The number of deaths in a given population during a given time frame in a given geographic area generally expressed per 100,000 population.
- Environmental Assessment .... Evaluation of the environment to identify an agent, or agents that may cause cancer.
- Epidemiology .....The study of the patterns, causes, and control of diseases in human populations.
- Etiological Study.....A study that attempts to determine the cause or causes of a specific disease or condition.
- Feasibility Study.....A determination as to whether all the needed elements (e.g., data, time, manpower, etc.) are available for completing an analytical study.
- Guidelines .....A written plan specifying the procedures to be followed in conducting research or an investigation.
- Latency or Latent Period .....The length of time between when a person is exposed to an environmental agent and the onset of the disease. May also refer to the period of time between the onset of risk factors and diseases they cause.
- Metropolitan Statistical Area (MSA) .....A Core Based Statistical Area associated with at least one urbanized area that has a population of at least 50,000. The MSA comprises the central county or counties containing the core, plus adjacent outlying counties having a high degree of social and economic integration with the central county as measured through community. Source: Federal Register / Vol. 65, No. 249 /
- Plausible .....Likely, believable or credible.
- Population .....The number of residents of a given geographic area.
- Population Estimates .....An estimate of the number of persons (by age and sex and for select counties race) living in Missouri and its 115 counties. Population estimates are produced and developed by analysts at DHSS using in large part inputs from the U.S. Census Bureau and the Federal State Cooperative Program for Population Estimates. **Or**, an estimate of the total population and population age groups for Missouri and its counties, prepared by the U.S. Census Bureau and Missouri Office of Administration under the Federal-State Cooperative Program for Population Estimates. Source: DHSS. *Population estimates*. Retrieved February 16, 2006 from <http://www.dhss.mo.gov/profiles/Population/PopulationEstimatesDefinition.htm>
- Prevalence .....The proportion (usually the percentage) of a population that has a defined risk factor, disease, or condition, at a particular point in time.
- p-value* ..... A measure of the probability that the results of an analysis were due to chance. For example, the probability that the results of a study are due to random chance less than 5% of the time would be written as  $p < 0.05$ .



- Rapid Case Ascertainment .....The process of identifying new cancer cases currently not in existing databases. Reporting facility staff searches their records for new reportable cases and submits them to the central cancer registry.
- Rate.....A rate is a ratio of those having the public health event of interest e.g., cancer) to the population of those at risk of having the given health event. Rates are calculated by dividing the number of events by the population at risk, or a related population, and then multiplying by a constant. The size of the constant depends on the rarity of the event being reviewed. Source: DHSS. *Rate*. Retrieved February 16, 2006 from <http://www.dhss.mo.gov/GLRequest/MCHRate.html>
- Robust.....The extent to which a statistical test yields essentially the same finding with a wide range of variations in performing the test. Related to statistical tests, robustness is a measure of a test’s strength in handling data and data errors without test failure.
- Standardized Rate .....A reference population is used as the standard population. The **standardized rate** is the sum of weighted group-specific **rates**, with weights derived from the standard population. The weights sum to 1.0. A **standardized rate** is essentially a weighted average of the age-specific **rates** Biological Plausibility A causal association (or relationship between two factors) is consistent with existing medical knowledge. Substances may produce illness in a variety of ways such as direct invasion, through the production of a toxin, allergic reaction, etc. This term refers to whether it is likely that a given substance caused the specific disease in a manner that is believable or possible.
- Standard Population .....Standard population – a set of arbitrary population weights whose proportions are used as the standard in adjusting rates for different groups in order to eliminate differences between their rates which are based on their composition. The National Center for Health Statistics recommends that the projected U.S. 2000 standard population be used when calculating age-adjusted rates. However, if you compare rates from different sources, it is very important that you use the same standard population on both sides of your comparison. It is not legitimate to compare adjusted rates that use different standard populations. Source: Anderson RN, Rosenberg HM. Age Standardization of Death Rates: Implementation of the Year 2000 Standard. National vital statistics reports; vol 47 no.3. Hyattsville, Maryland: National Center for Health Statistics. 1998, found at: [http://www.cdc.gov/nchs/data/nvsr/nvsr47/nvsr47\\_03.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr47/nvsr47_03.pdf) 2000 U.S. standard populations acquired from: Anderson RN, Rosenberg HM. Age Standardization of Death Rates: Implementation of the Year 2000 Standard. National Vital Statistics Reports; Vol. 47 No. 3. Hyattsville, Maryland: National Center for Health Statistics. 1998. The following are the U.S. standard population distributions in eleven age-groups:

Age	2000 Proportion
Under 1 year	0.013818
1 - 4 years	0.055317
5 - 14 years	0.145565
15 - 24 years	0.138646
25 - 34 years	0.135573
35 - 44 years	0.162613
45 - 54 years	0.134834
55 - 64 years	0.087247
65 - 74 years	0.066037

75 - 84 years	0.044842
85 and over	0.015508
All ages	1.000000

Statistically Significant.....Describes a mathematical measure of difference between groups. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone.

# References

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- <sup>10</sup> Breslow, N.E., & Day, N.E. (1987). *Statistical methods in cancer research: Vol. 2*. Lyon, France: International Agency for Research on Cancer