Rocky Mountain Arsenal Medical Monitoring Program Recommendation
Monitoring Cancer Incidence

I.   **Background**: Cancer is a variety of different diseases, rather a single adverse health outcome, characterized by uncontrolled growth and spread of abnormal cells.   Unfortunately, these diseases are common within the population, and therefore remains at the forefront of public health concern.

Coloradans have, on average, an individual lifetime risk of cancer of approximately one chance in three. An individual's personal experience is influenced by a variety of factors, not all of which are currently recognized. We do know that the development of cancer is a complex process involving both external (chemical, radiation, and viruses) and internal (hormonal, immune conditions, and inherited mutations) factors. Unfortunately, this complexity and its associated latencies severely limit our ability to identify causative factors or combination of factors. We may, however, monitor incidence rates so as to be alert to significant deviation from the expected background rates. This in turn allows us to investigate such deviations with respect to potential environmental associations.

This document describes the essential steps involved in data collection and analysis of cancer incidence in communities surrounding the Rocky Mountain Arsenal (RMA). Also addressed is the process by which appropriate follow-up investigations are selected.

II.   **Objectives:** Use the Colorado Department of Public Health and Environment's (CDPHE) existing cancer registry, the Colorado Central Cancer Registry (CCCR), to satisfy the following objectives for the communities surrounding the RMA:

Objective 1:   Determine which cancers tracked by the CCCR should be included in this cancer monitoring program.

Objective 2:   Establish baseline rates of cancer incidence.

Objective 3:   Describe and analyze cancer incidence rates for significant temporal changes during and after the RMA soil remediation.

Objective 4:   Describe and analyze spatial occurrence of cancer incidence during and after the RMA soil remediation.

Objective 5:   Use preestablished, scientifically sound criteria to determine the need for, and type of appropriate follow-up investigations, based on the findings of objectives 2, 3 and 4.

III.   **Population to be Addressed:** Residents within the approximate boundaries of 128th Ave., Gun Club Road, I-70, I-270, and the South Platte River. Actual boundaries may vary from those listed here if analyses are based on census tract and block groupings.

IV.   **Expertise Required:** CDPHE staff familiar with the CCCR, census data, temporal and spatial statistical analysis, geographic information systems (GIS), public health epidemiology, health education, and the RMA remediation and medical monitoring programs.

V.   **Strategy:**

    A.   Confidentiality

       Confidentiality of personal identifying information contained in the CCCR is strictly governed by State law and protocols are currently in place which assure compliance.

    B.   General Description

       Objective 1:   Determine which cancer sites currently tracked by the CCCR should be included in this cancer monitoring program.

       Reported cancer cases are categorized by the CCCR according to the International Classification of Diseases for Oncology , by anatomic site and histology. The initial objective of this program is to select specific cancers for surveillance based on biological plausibility or known associations with chemicals present at the RMA. In addition to any specific cancers, the incidence of all cancer combined will be monitored.

       Objective 2:   Establish baseline rates of cancer incidence.

       Prior to monitoring for changes in cancer incidence, baseline rates will be established. The CCCR has maintained complete reporting of cancer incidence in the Denver Metropolitan Area since 1979. Baseline rates will be established for the period 1979 to 1996. This time period will be examined for events which may influence ascertainment of cancer cases in the study area or comparison area (all of greater Denver). If such events are identified, the significance will be evaluated and appropriate measures taken to eliminate the undesired influence. Place of residence is registered by CCCR based on case address at the time of diagnosis. Baseline rates for existing residents of the surrounding communities may not be representative of all residential groupings if new communities are established during the RMA soil remediation. Additional comparisons will need to be identified for this special case.

       Objective 3:   Describe and analyze cancer incidence rates for significant temporal changes during and after soil remediation.

       Temporal changes in cancer incidence will be monitored for the period 1997 onward. The frequency of analyses will be determined in consultation with CCCR based on statistical considerations (number of new cases, ability to observe changes, completeness of reporting). The timing of the initial post-baseline analysis will take into consideration these same issues as well as latency.

Objective 4:   Describe and analyze spatial occurrence of cancer incidence during and after soil remediation.

The spatial distribution of cancer cases will be examined. Different methods will be evaluated to achieve this objective. The standard approaches of evaluating incidence by census tract and block group aggregates is a proven method and one which is consistent with prior cancer incidence investigations in the communities surrounding the RMA. Alternatively, the spatial scan method, already described in the Medical Monitoring Advisory Group (MMAG) recommendation *Surveillance for Birth Defects,* may be an effective approach. This methodology scans the case distribution over the geographic area of interest and provides the location of the most likely cluster for that data set.

Objective 5:   Use preestablished, scientifically sound criteria to determine the need for, and type of appropriate follow-up investigations, based on the findings of objectives 2, 3 and 4.

The design of this monitoring program is appropriate since the intent is to screen community cancer incidence. However, the study design has well-established limitations. This study is not expected to allow conclusions to be drawn about cause and effect relationships in the study population. Rather it allows public health officials to formulate new questions, based on unexpected departures from the norm, which can be addressed in "second-tier" or follow-up investigations of the type needed, for example, a case-control study. The process for selecting an effective follow-up study design or other public health action is described in the draft MMAG recommendation *Guidelines for Public Health Responses to RMA Related Exposure and Observations of Health Concerns Among Communities and Visitors*.

C.   Statistical Methods

Virtually all cancer cases diagnosed during the time periods and areas of interest are identified and registered with the CCCR. This identification process involves searching hospital medical charts, pathology laboratory records and examining death certificate information. Census counts by age and sex are obtained from the Colorado Division of Local Government (State Demographers Office). Average annual age-adjusted cancer incidence rates by gender for the Denver Metropolitan Area are available from the CCCR for comparisons and calculation of expected numbers of cancer cases. The expected number of cancer cases are calculated by multiplying the Denver Metropolitan Area's age and sex site-specific incidence rates by the age- and sex-specific population estimates.

Methods of data analysis are identified in this recommendation and are described in general terms below. Each will be carefully evaluated and the most effective method will be used.

1.	Observed/Expected Analysis

This method of analysis relies on the calculation of observed/expected ratios (O/E ratios) of cancer cases. Age and sex-specific O/E ratios for a particular cancer site, or grouping of sites, are calculated by dividing the number of diagnosed cancer cases by the expected number of cases for a specified time period. The O/E ratio may be considered a standardized incidence ratio (SIR). Mathematical formulas and statistics are used to further describe or clarify the association between the observed and expected numbers.

2.	CUSUM Analysis

The CUSUM analysis examines the frequency of cancer per unit time. This method will help to provide the earliest possible indication, a flag, of a shift away from the baseline rate, e.g., an increased rate, versus observing normal or expected fluctuation around a stable baseline rate of disease occurrence. These flags can be selected for specific cancer and all cancers combined and with an awareness of the sensitivity or power of the data and statistical methods to observe non-random changes in cancer frequency. In other words, before monitoring begins, a clear picture of the magnitude of change that can be detected and the ability of the system to detect them, must be determined in at least a semi-quantitative manner.

3.	Spatial Scan Analysis

A spatial scan analysis describes and analyzes the spatial occurrence of cancers in a community. By combining CCCR and GIS resources, mapping of the location of cancer cases may be possible. This capability directly addresses the public and scientific quandary of how to evaluate the frequency distribution of health outcomes, in this case, cancer, while minimizing the bias introduced by arbitrarily grouping these events within administrative or political boundaries. Once mapping is accomplished, analysts can then examine the data for possible non-random geographical occurrence, or statistically significant clusters. An appropriated statistical method for this analysis is the spatial scan statistic.

D.	Protocol Development

1.	Identify exact geographic boundaries for monitoring.
2.	Evaluate contaminants of concern for known or suspected carcinogenicity.
3.	Identify "all cancers combined" and select specific cancer sites.
4.	Confirm time periods for establishing baseline rates.
5.	Determine most effective and feasible analytical and statistical methods.
6.	Obtain appropriate data for selected analytical and statistical methods.
7.	Determine the periodicity of temporal analysis.
8.	Determine the boundaries/methods of spatial analysis.

VI.   Advantages and Limitations of this Proposal:

A.   Advantages

    1.   Reliable data sources already exist.

    2.   Baseline data are available for comparison to future data.

    3.   The ability to identify virtually all cancer cases in the communities surrounding the RMA.

    4.   Expertise in medical record review and disease investigation is already established in the Disease Control and Environmental Epidemiology Division and the CCCR of the CDPHE.

    5.   The methods proposed are consistent with prior investigations or improve on certain aspects of prior investigations

    6.   Provides for multiple levels of data review and tiered follow-up.

B.   Limitations

    1.   The geographic distribution of cancer outcomes is reported to the CCCR is based on residence at the time of diagnosis. While it is feasible to determine the history of residency for persons residing near the RMA, residence elsewhere at diagnoses but with a past history of residency near the RMA may be lost to follow-up.

    2.   As in all epidemiological investigations, a variety of factors influence observational ability.   Factors such as population size, normal frequency of a birth defect are examples of factors which will need to be considered when interpreting the findings of this plan.

    3.   The study design is not expected to allow conclusions to be drawn about cause and effect relationships in the study population. Rather, it allows public health officials to formulate appropriate follow-up based on initial data analyses.