Rocky Mountain Arsenal Medical Monitoring Program Recommendation
Remediation Monitoring - Medical Referral & Biomonitoring
Decision Tree

I. **Objectives:** Establish a logical progression of inquiry and response, hereafter referred to as the *Decision Tree*, as an aid the Medical Monitoring Program[1] in determining the adequacy of exposure prevention activities and for determining when the Program should consider implementing individual medical referral or community biomonitoring.

II. **Use of the Decision Tree:** The Decision Tree that follows and the specific references appended are intended as a framework for guidance in decision making in the event acute or chronic excessive fence line air concentrations are reported. The Decision Tree is intended for application to off-post residents. While the document is expected to be directly applicable to most situations encountered during Rocky Mountain Arsenal (RMA) remediation, it is also intended to be flexible and enable a protective and effective public health response to the risks associated with off-post exposure to Chemical of Concern (COCs)[2].

Specifically, it is recognized that the criteria for medical monitoring, as adopted by Agency for Toxic Substances and Disease Registry (ATSDR), describes one of several investigative and health education activities that represent appropriate follow up measures (see Strategy, Step 6). However, decisions by State and local health officials to deviate from the ATSDR criteria and use alternative approaches will be based on a sound scientific rationale. Other options for follow up measures might include, but are not limited to, surveys of community health, epidemiological studies, medical surveillance, or disease prevalence studies.

III. **Population to be Served:** Communities surrounding the RMA.

IV. **Systems Required:** This decision tree requires that supporting remedial and medical monitoring systems and criteria be operative. These systems are: A) Primary Prevention of Exposure, i.e., implementation of the air pathway analysis/remedial design and engineering and health protective fence line concentrations; B) Medical Referral System; and C) Medical Monitoring Criteria. Each of these systems are in place or are under development.

A. Primary Prevention of Exposure: Prevention of exposure and continuous evaluation of changing exposure conditions will result from carefully designed and implemented remedial activities. Activities are summarized below and described in greater detail in Attachment 1.

1. Atmospheric monitoring, both on-site and at the fence line, of COCs using a well designed system and sound quality assurance;

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[1] The RMA Medical Monitoring Program is being administered by the Colorado Department of Public Health and Environment.

[2] COC is used here and in the decision tree to refer to both COCs as well as other chemicals identified as potentially important contributors to health risk.

2. Characterization of the toxicological significance of an exposure concentration and duration using the Interactive Comprehensive-Air Pathway Analysis established site-specific acute and chronic fence line concentrations which are demonstratably protective of public health[3]; and

3. Exposure reduction relying on an appropriate remedial design including implementation of a environmental monitoring program and feedback of monitoring data to remedial managers charged with modification of remedial activities to protect public health.

B. Medical Referral System: The Rocky Mountain Arsenal Medical Monitoring Program has adopted the *Medical Referral System & Health Professional Education* plan[4]. The referral system will:

1. Assist medical providers serving communities surrounding RMA in addressing acute, subacute and chronic RMA-related health concerns; and

2. Assist persons residing or who have resided in these same communities in addressing their RMA remediation-related health concerns.

The design and purpose of this referral system is to ensure that the general population has an informed health care provider population and referral system to assist in the assessment of health concerns potentially related to the RMA remediation and any subsequent treatment.

C. Medical Monitoring Criteria: Preestablished criteria are necessary to determine the appropriateness of community biomonitoring.

1. Medical monitoring criteria have been established by ATSDR and are included here as Attachment 2[5]. These criteria are phased in their application. Phase I requires demonstration that significant exposure to a chemical agent is likely to have occurred and that there be a link between exposure and a specific health effect or a biological marker.[6]

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[3] Concentration at the fence line is a surrogate measure of potential exposure in the community. However, both fence line and on-site monitoring data will be available to evaluate emissions from contaminated media.

[4] The Medical Referral System may be accessed at any time by concerned citizens or their physicians as indicated in the RMA *Medical Referral System & Health Professional Education* plan; a contaminant concentration exceeding the respective site-specific acute or chronic fence line concentrations is not required. Appropriate medical response will be determined using referral system criteria and physician judgement.

[5] ATSDR's Final Criteria for Determining the Appropriateness of a Medical Monitoring Program Under CERCLA. FR 60 (145) 38840-38844. These medical monitoring criteria are a phased approach to determining the appropriateness of implementing a medical monitoring program under CERCLA. CERCLA defines medical monitoring as "the periodic medical testing to screen people at significant increased risk for disease."

[6] Information on the remediation-related exposure prevention activities in provided in Attachment 1 and may be useful knowledge when reviewing the ATSDR guidelines.

Phase II of the guidelines is the development of a site-specific medical monitoring plan which satisfies criteria designed to ensure that actions will be of public health benefit.

2. Complementary to the ATSDR Medical Monitoring Criteria, the RMA-MMAG Baseline/Human Health Monitoring Workgroup has developed criteria and a database specific to the RMA entitled *Clinical Measurement of Chemical of Concern Burdens for Chronic Exposure*. These criteria are used to determine the availability and feasibility of clinical measures for evaluating the presence of RMA COCs in human tissues. These criteria, and associated data, address the following topics and are presented in Attachment 3 of this document:

- Bioaccumulation and biological half-life
- Availability of suitable tissues for sampling
- Availability of standard methods, their specificity and detection limits
- Availability and type of biomarker

V. Strategy:

A. Prevention and Evaluation of Site Emissions: The following six-step decision tree should be used in the context of primary prevention activities to evaluate potential site emission scenarios or actual releases to determine the appropriate application of individual medical referral or biomonitoring in the community surrounding the RMA (see also Figure 1).

Step 1. Is an RMA COC detected at the fence line?
No -----> Maintain primary prevention
Yes -----> Go to Step 2

Step 2. Is the fence line level of the RMA COC in excess of fence line acute[7] or chronic[8] toxicity concentration?

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[7] An acute fence line air concentration is an ambient air concentration at the fence line that is not likely to cause adverse effects in an exposed human population, including sensitive subgroups. Exposure to a fence line concentration may occur on an intermittent basis. The uncertainty around this value may span an order of magnitude. An intermittent acute exposure to this concentration is defined as being of a duration of less than or equal to 24 hours and is assumed to occur no more frequently than monthly. The length of time between exposures should be greater for chemicals with a clearance time approaching one month or that have a cumulative effect or are sensitizers. This definition allows treatment of acute exposures as independent events and distinctly different from chronic low-level exposures.

[8] A chronic fence line air concentration is an ambient air concentration, for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects. This concentration is designed to be protective for exposures lasting a lifetime. Uncertainty around this value may span an order of magnitude or greater. In the case of potential carcinogens, the fence line concentration is an ambient level based on the upper-bound estimate of the probability of a response per unit dose of a chemical over a lifetime which will not produce a significant elevation in cancer risk. The target risk criteria used to establish fence line

No -----> Maintain primary prevention
Yes -----> Go to Step 3

concentrations of potential carcinogens is 10^{-6}, or one chance in one million.

Step 3. Define concentration and duration, implement a predefined Air Monitoring Data Review, Consultation and Decision Making Protocol[9], control air emissions through altered remediation and proceed to Step 4.

Step 4. Does the level of the COC detected exceed acute fence line concentration?
No ----> Go to Step 5
Yes ----> Go to Step 6

Step 5. COC exceeds chronic fence line concentration and may continue.[10]
No -----> Maintain primary prevention
Yes -----> Go to step 6.

Step 6. If the COC detected exceeds an acute fence line concentration, implement medical referral[11]

If the COC detected exceeds chronic fence line concentration and will continue uninterrupted for a prolonged or chronic duration, determine the appropriateness of community medical monitoring by referring to the following documents as guidelines:

a. ATSDR Medical Monitoring Criteria, and

b. MMAG criteria for Clinical Measurement of COC Burdens for Chronic Exposure.

The most effective, meaningful and responsive public health action will be dependent on a variety of toxicological and public health factors, and the determination of this action will require professional judgement. Alternative actions may include health outcome studies or additional exposure and epidemiological studies and professional education.

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[9] An outline of the recommended "Air Monitoring Data Review, Consultation and Decision Making Protocol" is provided in Attachment 1 to this document.

[10] Chronic exposure is generally accepted as referring to those of 7 or more years duration. The term "prolonged" is used here to acknowledge that exposure is the product of concentration and duration and therefore an exposure exceeding the respective site-specific fence line concentration with a duration of less than 7 years will be evaluated in light of the degree of the excess. This relationship can be similarly applied to both carcinogens and non-carcinogens.

[11] Services obtained as a result of medical referral for acute exposure may include individual medical testing and follow up, as determined by the attending physician.

Acute fence line concentrations may be applied at the fence line to address community exposure, or in the RMA interior to address on-post visitors. In either case, they are appropriately applied to short-term exposures. Occupational standards may be applied to on-post visitors, however, they may be less protective than the acute fence-line concentrations. Occupational short-term exposure limits are more appropriate for short-term visitors than occupational time-weighted averages. The decision tree, as applied to on-post visitors, calls for implementation of the Medical Referral System if visitors are exposed to air contaminants at concentration that exceed acute criteria (see Figure 2).

B. Evaluation of Health Concerns and Outcomes: In addition to the process for evaluating site emission scenarios or actual releases, both medical and epidemiological tools and skills are required to evaluate the significance of individual and community health and its potential association with the RMA. Medical diagnosis by physicians will be used to determine the identity and etiology of a disease or condition in an individual. Epidemiology will be used to evaluate disease etiology by investigating the distribution of disease in the community.

Medical and epidemiological tools will be used to evaluate individual and community health concerns, as described in the Medical Referral System & Health Professional Education and Surveillance for Birth Defects and Cancer Surveillance recommendations. In brief, the steps are (see Figure 3):

1. Individual case evaluation by the RMPDC

2. Case reporting to CDPHE - A standard reporting format and frequency will be established by RMPDC and CDPHE.

3. RMPDC and CDPHE have the responsibility to collaborate to identify individual suspect cases and multiple case patterns and trends through an analysis of:

    a. Signs and symptoms and diagnostic test results
    b. Cumulative exposure and/or risk
    c. Frequency of reporting
    d. Temporal distribution
    e. Spatial distribution
    f. Environmental and other relevant factors

    RMPDC and CDPHE also have the responsibility for initiating more detailed case investigations if warranted by initial information.

Attachment 1

Primary Prevention and Air Monitoring Data Review, Consultation and Decision Making Protocol

Primary Prevention and Air Monitoring Data Review, Consultation and Decision Making Protocol

Air Pathway Analysis

Primary prevention of site-related off-post exposure will be managed through the use of the Interactive Comprehensive-Air Pathway Analysis (IC-APA) in construction design. The IC-APA is using site-specific soil contamination and air emission potential data, meteorological data and contaminant transport modeling of contaminant emission concentrations at downwind locations. By limiting the acceptable fence line concentration, an allowable emission source term can be estimated, on a site-specific basis, which will be used to determine an acceptable rate and extent of soil remediation.

Fence line monitoring data will be used to confirm that air emissions due to excavation and removal of soils do not exceed target risk levels at the fence line. These monitoring data will also be used to validate and improve the performance of the IC-APA. Additionally, on-site monitoring technology will facilitate IC-APA estimation of fence line concentrations during an excavation.

Continuous chemical-specific real-time fence line monitoring data will not be available as a rule. However, the combination of site-specific data, the IC-APA, and on-site and fence line monitoring is expected to result in preremedial designs and ongoing design modifications that will control fence line concentrations consistent with target risk goals.

Fence Line Concentrations

Fence line concentrations are being set at levels which will be protective of public health.
For known or potential carcinogens, a risk goal of 10^{-6} (one chance in one million)[1] will be used at the RMA fence line during remediation. For non-cancer chronic and acute health effects, the goal is a risk ratio of 1. The APA work group is completing a list of RMA site-specific air emission concentrations that meet these goals for COCs. Additional health-protective concentrations will be developed for important non-COCs risk contributors on a site-specific basis. Fence line concentrations in excess of the target risk concentrations will trigger a performance evaluation to determine the cause and what corrective actions, if any, are appropriate.

Air Monitoring Data Review, Consultation and Decision Making Protocol

The RVO, local, State and Federal public health officials each have responsibilities related to the ongoing review of on-site and fence line monitoring data (see attached Air Monitoring Data Review and Decision Process flow diagram). Although governmental health and environmental protection agencies have legally mandated public health responsibilities, the RVO too shares this obligation to the community. While the

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[1] For a few chemicals, the background concentration near the fence line due to non-RMA sources may exceed 10^{-6}. In the case of a measurement in excess of the target risk level for these chemicals, upwind versus downwind concentrations will be examined and analytical and statistical information will be considered to determine whether it is an RMA issue.

RVO's primary responsibility is management of site remedial activities, the RMA Record of Decision[2] identifies CDPHE and ATSDR as the agencies responsible for conducting the Medical Monitoring Program including interpreting the medical monitoring-related significance of excess fence line concentrations. Therefore, judgement of the public health significance of air monitoring data and the appropriate response will be made through a collaborative partnership among the responsible parties, not by the RVO alone[3].

- The purpose of this collaboration is to maintain vigilance and reporting of departures from modeled and acceptable fence line concentrations.

- This review and reporting process will be independent of construction management.

- Reporting of excess concentrations at the fence line or at the exclusion zone will be made to an RVO official responsible for public health protection and with the authority to require a determination of the cause and modifications of site remedial activities.

- Reporting will also be made to local, State and Federal public health officials who will be responsible for providing consultation to the RVO on the health significance of concentrations and exposure duration.

- The RVO and public health officials will work collaboratively to determine a proper response to COC fence line concentrations in excess of health protective levels established as part of the Air Pathways Analysis. However, the RVO will defer to public health officials regarding medical monitoring issues and other public health actions in these matters. In the event that CDPHE is not in agreement with the health protectiveness of RVO actions, CDPHE maintains the ability to seek timely resolution through an existing dispute process or specifically mandated public health authority.

This process will be set out in protocol prior to the beginning of project-specific remedial activities. The protocol will include a detailed decision tree defining appropriate response actions offering responsible flexibility under differing scenarios which will eliminate additional excursions above the health protective fence line concentrations.

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[2] Record of Decision (June 1996), Section 9.4.

[3] In addition to air monitoring data review by the RVO and governmental agencies, data packages will also be available to the public. The public need for this information, and the design of data delivery, will be addressed in the MMAG Environmental Monitoring Subcommittee recommendations.

Attachment 2

ATSDR's Final Criteria for Determining the Appropriateness of a Medical Monitoring Program Under CERCLA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Toxic Substances and Disease Registry

[ATSDR–96]

ATSDR's Final Criteria for Determining the Appropriateness of a Medical Monitoring Program Under CERCLA

AGENCY: Agency for Toxic Substances and Disease Registry (ATSDR), Public Health Service (PHS), Department of Health and Human Services (HHS).

ACTION: Notice.

SUMMARY: This notice announces the criteria for determining the appropriateness of a medical monitoring program under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). Draft criteria were published for public comment on September 9, 1994 (59 FR 46548). The public comment period ended October 24, 1994. Comments were received from 15 individuals representing States, industry, activist groups, and environmental medicine clinics. This document reflects those comments received on the draft criteria.

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FOR FURTHER INFORMATION CONTACT: Dr. Wendy E. Kaye, Chief, Epidemiology and Surveillance Branch, Division of Health Studies, ATSDR, telephone (404) 639–6203.

SUPPLEMENTARY INFORMATION: Section 104(i)(9) of the Comprehensive Environmental Response, Compensation, and Liability Act [CERCLA], as amended [42 U.S.C. 9604(i)(9)], provides for the Administrator of the Agency for Toxic Substances and Disease Registry (ATSDR) to initiate a health surveillance program for populations at significantly increased risk of adverse health effects as a result of exposure to hazardous substances released from a facility. A program included under health surveillance is referred to as "Medical Monitoring or Screening" by ATSDR and is defined in the legislation as "the periodic medical testing to screen people at significant increased risk for disease." ATSDR has established criteria to determine when medical monitoring is an appropriate health activity and the requirements for establishing a medical monitoring program at a site. The legislation also states that a mechanism to refer people for treatment should be included in the program. Statutory language only allows ATSDR to provide medical care or treatment in cases of public health emergencies as declared by the President.

Background

ATSDR is responsible for the public health-related activities of CERCLA. ATSDR's primary initial response at a hazardous waste site is the public health assessment, which is required for every site on the National Priorities List (NPL). A public health assessment can also be conducted in response to a petition from the public. Other important components of ATSDR's initial response at sites include health consultations and public health advisories. During the process of developing the public health assessments and health advisories, ATSDR invites the participation of communities through a variety of avenues such as public meetings, public availability sessions, and Community Assistance Panels (CAPs). The documents produced by ATSDR during the process are placed in a public repository to allow the public access to the documents. The public health assessments, health consultations, and public health advisories undergo review by ATSDR to determine if follow-up health-related activities are needed for populations at risk in the affected community.

The types of follow-up health activities recommended for a site will depend on the amount of information on the possible exposures and their suspected pathways. In any case in which an association has not been established between an exposure and a specific adverse health outcome, several research and health education activities may be considered. Those activities could include health outcome studies, an exposure assessment at the site, epidemiologic studies, or professional education.

ATSDR's Division of Health Assessment and Consultation has established a program for the investigation of exposures in communities which enables a more timely response to questions on whether individuals in a community are being exposed. The program incorporates a variety of industrial hygiene techniques for measuring chemicals in the environment, as well as selected biological markers of exposure.

The Division of Health Education provides a wide variety of services to educate health care professionals and communities on the effects of exposures to hazardous substances. Activities in a community around a hazardous waste site may include conducting grand rounds for health care providers on the effects of a specific chemical, providing fact sheets on chemicals, conducting workshops on clues to environmental disease, and producing case studies in environmental medicine.

The Division of Health Studies is responsible for conducting epidemiologic research, including several types of studies (cluster investigations, disease and symptom prevalence studies, analytic epidemiologic studies), surveillance programs, and exposure registries. Cluster investigations and disease and symptom prevalence studies investigate the occurrence of disease in populations. Analytic epidemiology studies are conducted to evaluate the causal nature of associations between exposure to hazardous substances and disease outcomes. The surveillance program focuses on exposures to substances at hazardous waste sites and includes systems that follow populations exposed to hazardous wastes because of where they live or their occupation. It also includes surveillance of emergency events in which hazardous substances are released into the environment. The National Exposure Registry maintains a listing of people exposed to hazardous substances. The Registry is composed of chemical specific subregistries. The chemicals are selected from the ATSDR/EPA priority list of hazardous substances.

Medical monitoring is considered one of several follow-up health activity options under the site-specific work conducted by ATSDR. A medical monitoring program for the community around a site will be considered with other health follow-up activities when the information from ATSDR's initial response at the site is reviewed. In cases in which there is no known association between the exposure and specific adverse health effects (which could include health outcomes, illnesses, or markers of effect), medical monitoring is not an appropriate public health activity. In cases in which there is limited information on a specific health effect's relationship to an exposure, then options such as epidemiologic surveillance, a disease and symptom prevalence study, or an epidemiologic study are more appropriate. When adequate information exists that links exposure to a chemical with a specific adverse health effect, further consideration will be given to the appropriateness of medical monitoring in that population.

Medical monitoring should be directed toward a target community identified as being at "significant increased risk for disease" on the basis of its exposure. Significant increased risk will vary for particular sites depending upon such factors as the underlying risk of the selected outcome, the risk attributable to the exposure, and the presence of sensitive subpopulations. These factors will be considered when evaluating the appropriateness of medical monitoring in a community. The CERCLA legislation also provides for a mechanism for referral for treatment of those who are screened positive for the selected health outcomes; therefore, a mechanism to refer people for diagnosis, interventions, or treatment should be in place prior to the initiation of a medical monitoring program.

The primary purpose of a medical monitoring program is not considered to be a research activity that further investigates the cause-effect relationship between exposure and outcome. The purpose of a medical monitoring program is case-finding in order to refer individuals for further evaluation and, as appropriate, treatment. Within this framework, medical monitoring includes both testing for early biological effect and an assessment of exposure using biological specimens (for example, blood or urine), when appropriate. This is provided as a service to individuals in communities where there is believed to be an increased risk of disease from exposure to hazardous substances released into the environment.

Criteria for Considering Medical Monitoring

The criteria outlined below will be used to determine the appropriateness of conducting medical monitoring in a community and will be applied in a phased approach. Phase I, conducted by ATSDR, consists of an evaluation of the exposure and outcome criteria. Phase II consists of an evaluation of the system criteria. Phase II will be conducted with the input of a panel consisting of community, State and local health officials, and ATSDR. At the end of Phase II, a detailed medical monitoring plan will be written at sites where a monitoring program is established. All of the criteria must be met at a site in order for a medical monitoring program to be established at that site. In addition, resources must be available to initiate and sustain the program.

Phase I

Exposure Criteria

A. There should be evidence of contaminant levels in environmental media that would suggest the high likelihood of environmental exposure to a hazardous substance and subsequent adverse health outcomes.

The National Research Council (NRC) defines exposure as "an event that occurs when there is contact at a boundary between a human and the environment at a specific contaminant concentration for a specified period of time; the units to express exposure are concentration multiplied by time" (NRC, 1991). The specific contaminant concentration and period of time will vary for different chemicals and different media. The exposure must be to a hazardous substance as defined under CERCLA, and the result of a release from a CERCLA-covered facility. A release from a CERCLA-covered facility includes those events that establish an open pathway of exposure (i.e., an unfenced area with high soil contamination could be considered a "release") or allows contaminants to go off-site via air, surface water, ground water, or other pathway. The primary criteria for medical monitoring should be documented evidence of exposure of a population to a hazardous substance in the environment. An exposure will be considered to be at a sufficient level if there is documentation of an increased opportunity for exposure to a level that meets or exceeds some health-based comparison value (such as Minimum Risk Levels (MRLs) or Reference Doses (RfDs)) or that meets or exceeds a level reported in the peer-reviewed literature to result in some adverse health effect. Documentation is considered sufficient if it is from an exposure assessment, environmental exposure modeling, or sampling from a general area (for example, water samples from an aquifer or a town water supply). Documentation of individual levels of exposure is not required. In cases in which exposures are unknown or undocumented, environmental monitoring is a more appropriate initial activity.

B. There should be a well-defined, identifiable target population of concern in which exposure to a hazardous substance at a sufficient level has occurred.

Initially, the target population of concern will be defined geographically on the basis of exposure. In addition, all populations considered will be assessed for the presence of any sub-population at increased risk of the adverse health effects associated with the exposures. An example of a subpopulation at increased risk would be preschool children in an area with known lead exposures. The size of the target population of concern is not a factor in the decision for monitoring. In areas where biological markers of exposure have not been collected, environmental sampling can be used to estimate exposure levels. The target population of concern is the population in which there is documented exposure at a sufficient level to place the individuals in that population at significant increased risk for developing some specific adverse health effect.

Outcome Criteria

A. There should be documented human health research that demonstrates a scientific basis for a reasonable association between an exposure to a hazardous substance and a specific adverse health effect (such as an illness or change in a biological marker of effect).

Previous studies on human populations must demonstrate a reasonable association between a particular exposure and an adverse health effect. In order to make that inference, consideration should be given to the strength, specificity, and consistency of the association among the identified studies. The period of exposure (including the timing and duration of the exposure) and its relationship to the latency period for the disease or illness should also be examined if information is available. Consideration should be given to whether the association has demonstrated a dose-response relationship and whether the association is consistent with the existing body of knowledge. This information could include a variety of occupational, epidemiological, or other studies involving human populations.

B. The monitoring should be directed at detecting adverse health effects that are consistent with the existing body of knowledge and amenable to prevention or intervention measures.

The monitoring should be established for specific adverse health effects. The specific adverse health effect being monitored should be a result of the possible exposure consistent with the existing body of knowledge. An adverse health effect is consistent with the existing body of knowledge if it has been described in the literature as caused by that agent or by similar agents, taking into account structure-activity relations.

In addition, the adverse health effects (disease process, illness, or biomarkers of effect) should be such that early detection and treatment or intervention

interrupts the progress to symptomatic disease, improves the prognosis of the disease, improves the quality of life of the individual, or is amenable to primary prevention. If the adverse health effects that are of concern in an individual or in a community are not easily detectable and not medically treatable, then medical monitoring would not be beneficial and would not be an appropriate public health activity. An easily detectable effect is one that can be found on clinical examination, or through the use of simple, diagnostic tests in an outpatient setting. Also, the test procedures must be acceptable to the patient and the community. The diagnostic tests must be nonexperimental, relatively noninvasive (such as the drawing of a tube of blood for laboratory tests), and simple to administer.

Monitoring for Evidence of Continuing Exposure

At sites with exposure in the community, the monitoring program might include biological markers of continuing exposure. For example, the Bunker Hill Superfund site has had lead screening of children for many years. Those sites would be ones in which the exposure is known to have a variety of adverse health effects, but for which no tests are available to detect those effects at a time when intervention could affect the course of the disease process. In those instances, the primary intervention is to remove the individual from the exposure. This allows the medical monitoring system to recommend referral for intervention prior to the onset of detectable adverse health effects. A monitoring system that includes biomarkers of continuing exposure is similar to medical surveillance of hazardous waste workers where changes indicative of increasing or continued exposures occur sufficiently early that the exposure can be curtailed and the risk for disease reduced (Gochfeld 1990).

Phase II

General Information

Phase II of the program is carried out by ATSDR with assistance from the community. When ATSDR has determined that exposure from a site has met the exposure and outcome criteria, a site panel will be formed based on recommendations from the community and the State and/or local health departments to review the system criteria and to assist in the development of a site-specific medical monitoring plan. The site panel will include representatives from ATSDR, the community, State or local health departments, local medical societies, and subject experts as necessary. The site panel will function in much the same manner as the Community Assistance Panels (CAPs) that are established at some sites during the public health assessment process. The site panel will follow the established procedures for those CAPs. The site panel will be responsible for assessing the available community health resources and determining the feasibility and extent of the screening program for the community. If the panel determines that a screening program is feasible in the community and ATSDR concurs with that decision, ATSDR will develop a site-specific monitoring plan. That plan will be presented to the site panel for review and concurrence. After the plan has been developed and has undergone peer review, it will be presented to the community at large for their input prior to establishing the program.

System Criteria

A. The general requirements for a medical screening program should be satisfied.

The monitoring aspect of a health surveillance program consists of the periodic medical testing to screen individuals who are at increased risk of disease. Monitoring serves to identify those individuals with an unrecognized adverse health effect. This is consistent with the definition of screening as "the presumptive identification of unrecognized disease or defect by the application of tests, examinations, or other procedures which can be applied rapidly. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment." (Commission on Chronic Illness, 1957) In general, the ability to predict the presence or absence of disease from test results depends on the sensitivity and specificity of the test and the prevalence of the disease in the population being tested. The higher the prevalence, the more likely a positive test indicates disease (Mausner & Kramer, 1985). In order for a screening program to be of public health benefit, the population being screened should be at a significantly high risk for the undiagnosed disease (i.e., the disease should have a sufficiently high prevalence in the population).

Given that definition, there are certain requirements for screening programs that should be considered when evaluating a possible medical monitoring program for a site (adopted from Mausner & Kramer, 1985). Those requirements are:

★ The natural history of the disease process should be understood sufficiently for screening.

★ The early detection through screening should be known to have an impact on the natural history of that disease process. For example, the detection of breast cancer while it is localized has been shown to increase the ten-year survival rate. For that reason, several groups have made recommendations for the early detection of breast cancer in asymptomatic women. Those recommendations include breast self-examination, breast physical examination, and mammography (Mettlin & Dodd, 1991; Kelsey & Gammon, 1991).

★ There should be an accepted screening test that meets the requirements for validity, reliability, estimates of yield, sensitivity, specificity, and acceptable cost. The purpose of ATSDR-sponsored medical monitoring is not to develop new screening tests. The medical monitoring program will use tests that have been recommended and used for screening in other settings.

The U.S. Preventive Services Task Force has established criteria for determining the effectiveness of preventive strategies including screening tests. The criteria for effectiveness of a screening test include the efficacy of the screening test and the effectiveness of early detection. The Task Force used efficacy to mean accuracy and reliability. The accuracy is measured using four indices: sensitivity, specificity, positive predictive value, and negative predictive value (see table below for definitions). A test with poor sensitivity will result in a large proportion of persons with disease being told they are free of disease (false-negatives). A test with poor specificity will result in healthy persons being told they have the disease (false-positives). There may be serious consequences in the use of screening tests with poor sensitivity and/or specificity. Persons with false negative results may have delays in diagnosis and treatment. False positive results can result in follow-up testing that is uncomfortable, expensive and potentially harmful. The evaluation and selection of a screening test must include a determination of the likelihood of producing false positive results (the positive predictive value (PPV)). The PPV changes in accordance with the prevalence of the condition in the screened population. PPV is unlike

sensitivity and specificity in that it is not a constant characteristic of a screening test. If the condition is sufficiently rare in the screened population, even tests with excellent sensitivity and specificity can have low PPV, having more false positive results than true positive results.

Another important aspect in determining the efficacy of a screening test is the reliability of the test. The reliability (reproducibility) is the ability of the test to give the same result when it is repeated. An accurate test with poor reliability can produce results that vary widely from the correct value, even though the average of the results approximates the true value. Poor reliability may be due to either interobserver variation or intraobserver variation (U.S. Preventive Services Task Force, 1989).

DEFINITION OF TERMS

Term	Definition	Formula*
Sensitivity	Proportion of persons with the condition who test positive.	a / a + c
Specificity	Proportion of persons without the condition who test negative.	d / b + d
Positive Predictive Value	Proportion of persons with positive test who have condition.	a / a + b
Negative Predictive Value	Proportion of persons with negative test who do not have the condition.	d / c + d

*Explanation of Symbols	Condition absent	Condition present
Positive Test	a	b
Negative Test	c	d

Legend: a=true +; b=false +; c=false −; d=true −.

★ The screening program should be one that is feasible and acceptable to individuals and the community. Therefore, plans and possible screening tests for a medical monitoring program will be presented to the community for input prior to the initiation of any recommended program.

B. An accepted treatment, intervention, or both, for the condition (outcome or marker of exposure) must exist and a referral system should be in place prior to the initiation of a medical monitoring program.

There should be established criteria for determining who should receive referral for intervention or treatment. These criteria will be based on the selected effect being screened for and the screening test being used. Results will be evaluated by ATSDR longitudinally and cross-sectionally to identify changes in the system or screening tools that require follow-up [Gochfeld 1990]. A referral mechanism should exist so that those who are eligible for the intervention can be referred to a qualified health care provider for further diagnosis, treatment, or intervention. The referral must be for treatment or intervention that is standard practice and not experimental in nature. The medical monitoring (screening) program is not responsible for the cost of the referral, the intervention, or the treatment of individuals participating in the program.

C. The logistics of the system must be resolved before the program can be initiated.

After medical monitoring has been determined to be appropriate for a site, the specifics of the monitoring system will be detailed in a site-specific medical monitoring plan. The site panel consisting of the community members, appropriate health officials, and subject experts as necessary will work with ATSDR to develop and review the site-specific medical monitoring plan. The specifics of the medical monitoring system recommended can vary for each site. The monitoring plan is the protocol for the specific program to be proposed in a community. The plan will outline the target community, the types of outcomes to be screened for, the participants in the referral system, and the program reports. The plan will include a review of the latency period for the outcomes being monitored and the duration of the exposure to define the period of time that the program will operate in a specific site population. The target population; the completeness with which the exposed population can be identified, contacted, and followed; the screening tests; and the selected health outcomes will all influence the specifics of the system. Existing medical facilities and personnel will be used when possible.

The monitoring plan will be submitted for peer review prior to its implementation at a site. The plan for a site might require additional review by an expert panel [ethicists, NRC] to evaluate the screening tests recommended. ATSDR's Division of Health Studies will work closely with the Division of Health Education to provide professional health education when needed to enhance the medical monitoring program.

Medical monitoring is one of ATSDR's service activities and is not considered to be a research tool. The monitoring activity at each site will be routinely evaluated for the effectiveness of the screening tests in place and the types of effects being detected. Due to confidentiality issues in dealing with small groups of people, the reporting from the system will consist of annual reports noting the number of individuals screened, the number of referrals made, and the number of conditions diagnosed in the referral system. ATSDR will develop a list that includes information on the types of exposures seen in the communities and the types of screening tests that were included in the monitoring. ATSDR can provide this information as available to the site panels to assist them in deciding on the types of screening tools based on what has been used in other areas.

The referral system will consist of the review of the screening results and the referral to appropriate health care providers or referral physicians. The specific mechanisms for determining who needs referral and for selecting the health care providers in the referral pool must be in place prior to the initiation of the medical monitoring. Once the participant has been referred to the

referral providers, those providers will be responsible for any subsequent diagnosis, treatment, or intervention.

Summary of Medical Monitoring

Medical monitoring will be considered along with the other health follow-up activities to be recommended for populations around specific sites. The Division of Health Studies will make a determination on whether a site meets the exposure and outcome criteria for medical monitoring. If a site meets the previously discussed criteria and is selected for further consideration of a medical monitoring program, ATSDR will work with the community and other appropriate entities in designing the specific monitoring and referral system for that site's target population. ATSDR will notify, and where appropriate, work with the state health department to establish the program. The Division of Health Studies will monitor the program and be responsible for the oversight on the annual reports.

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Dated: July 24, 1995.

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[FR Doc. 95–18570 Filed 7–27–95; 8:45 am]

BILLING CODE 4163–70–P

Attachment 3

Rocky Mountain Arsenal Medical Monitoring Program

Clinical Measures of COC Burdens for Chronic Exposure and Related Data

Rocky Mountain Arsenal Medical Monitoring Program
Clinical Measures of COC Burdens for Chronic Exposure

Complementary to the ATSDR Medical Monitoring Criteria, the RMA-MMAG Baseline/Human Health Monitoring Workgroup has developed criteria and a database specific to the RMA for *Clinical Measurement of Chemicals of Concern Burdens for Chronic Exposure*. These criteria are used to determine appropriate clinical measures of evaluating the presence of RMA COCs, used here to refer to both COCs as well as other chemicals identified as potentially important contributors to health risk) in human tissues[1].

1. Does the COC bioaccumulate and what is its biological half-life?

The COC's capacity for bioaccumulation must be present for the other data requirements to be useful. Bioaccumulation increases the likelihood that the chemical will be present in a body compartment long enough and in high enough concentrations as to be measurable at the time the appropriate tissue is collected. Therefore, if the COC is rapidly eliminated, it is not useful for biomonitoring.

2. What tissues can be reasonably sampled?

For a biomonitoring technique to be appropriate for use in a community health program, it must not be unduly invasive. Obtaining the specimen must not place the human subject at any unnecessary significant health risk, must be acceptable to the vast majority of potential subjects and must yield information which will significantly benefit the individual and/or community.

3. What established/standard methods are available?
- **Are these methods chemical- or chemical class-specific?**
- **What are the corresponding detection limits?**

Methods applicable to the tissue and COC in question must be available. A method should be standardized and well established so as to produce reliable and acceptable residue measurements. The method must not be experimental or of uncertain validity. Method detection limits should be low enough so as to observe biological concentrations likely to be present under the expected exposure conditions. Methods must also be adequately specific to ensure a low frequency of false positive or negative results.

4. Is the biomarker a direct or indirect indicator of exposure?

Whether the biomarker measured is a direct or indirect indicator of exposure, there must be sufficient toxicokinetic data to understand the relationship between the concentration of the species measured and the anticipated response.

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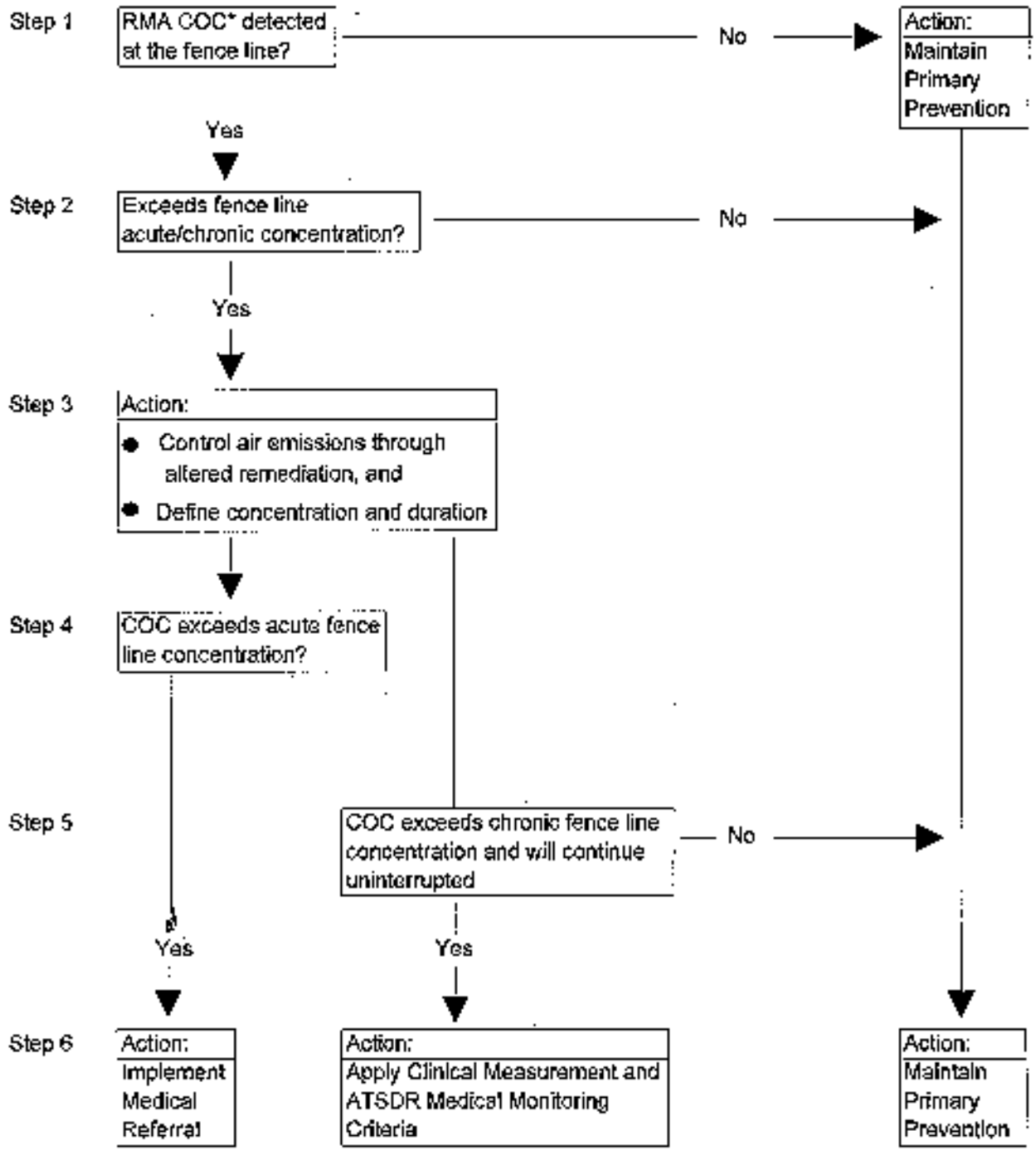
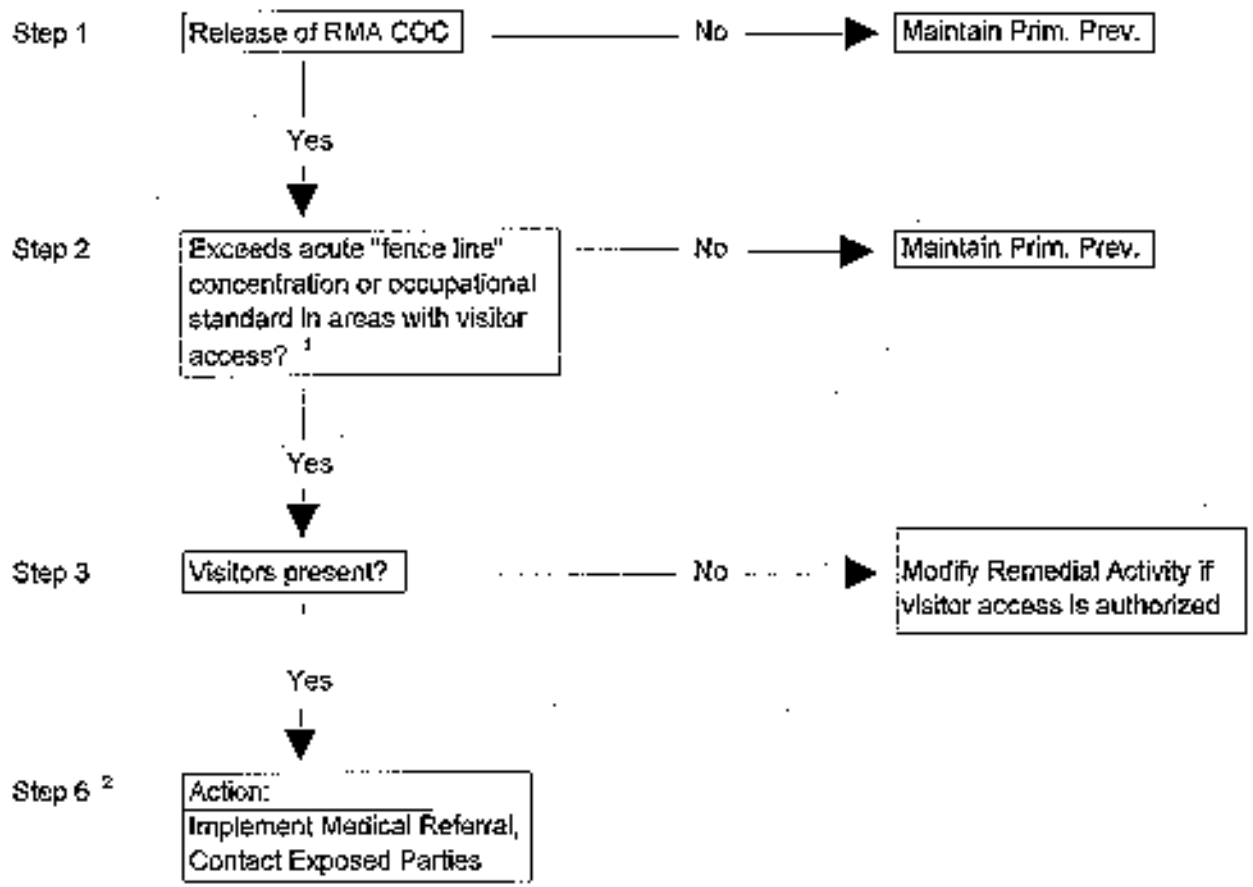
[1] The feasibility and acceptability of any type of biomonitoring activity is contingent on obtaining the cooperation of the community. Collection of any biological specimen from an individual requires obtaining the individual's informed consent.

FIGURE 1
MEDICAL REFERRAL & BIOMONITORING DECISION TREE
Air Monitoring Data



*COC is used in this document to refer to both COCs as well as other chemicals identified as potentially important contributors to heath risk.

Figure 2
Medical Referral & Biomonitoring Decision Tree
On-post Visitors



[1] Acute fence line concentrations may be applied at the fence line to address community exposure, or in the RMA interior to address on-post visitors. In either case, short term exposures are at issue. Occupational standards may be applied to on-post visitors, however, they may be less protective than the acute fence line concentrations. Occupational short-term exposure limits are more appropriate than occupational time-weighed averages.

[2] For Steps 4 and 5, see Decision Tree document.

Figure 3
MEDICAL REFERRAL & BIOMONITORING DECISION TREE
Case Reporting - Referral System