

Appendix 7

Final Protocol

Southeast Kansas Health Study

SOUTHEAST KANSAS HEALTH STUDY

FINAL PROTOCOL

January 1999

EPA ASSISTANCE AGREEMENT

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Duration: 09/01/97 through 9/30/00

Budget: \$650,000

**Center for Environmental and Occupational Health
1033 Breidenthal Building
The University of Kansas Medical Center
3901 Rainbow Boulevard
Kansas City, Kansas 66160-7417**

II. Table of Contents

I.	Title Page	1
II.	Table of Contents	2
III.	Narrative Statement	3
IV.	Study Background and Rationale.....	5
V.	Applicant Background	6
VI.	Study Work Plan	8
	A. Study Objectives	8
	B. Project Results/Benefits Expected	8
	C. Study Approach.....	9
	1. Project Accomplishment.....	9
	2. Facilities	17
	3. Non-federal Funding Sources and Facilities.....	20
	4. Chronological Schedule of Project Accomplishments	21
	5. Staff, Supporting Agencies, Consultants, and Contractors.....	24
	6. Data Collection, Analysis, and Evaluation	27
	Environmental Data	27
	Epidemiological Data.....	28
	Respiratory Health Data.....	28
	D. General Program/Project Information.....	29
	1. Data to be Collected.....	29
	2. Effect or Relationship of Program to Other Organization Work.....	31
	3. Federal, State, Interstate, and Local Programs to be Coordinated With Project	31
	E. Itemized Budget.....	32
	F. Human Subjects Protocol	34
	G. Quality Assurance Requirements	40
	H. Biographical Sketch of the Project Manager - H. William Barkman, M.D.	40
Appendices		
	A. Environmental Monitoring Assessment Quality Assurance Project Plan	
	B. Respiratory Health and Cancer Incidence and Mortality Rates Quality Assurance Project Plan	
	1. Letter of Information for Respiratory Health Questionnaire	
	2. Instructions for Completing Respiratory Health Questionnaire	
	3. Adult Consent Form for Respiratory Health Questionnaire	
	4. Parental Permission Form/Child’s Assent Form	
	5. Adult Respiratory Health Questionnaire	
	6. Children’s Respiratory Health Questionnaire	
	7. Consent Form for Participants in Study’s Respiratory Health Medical	
Evaluation		
	8. Initial and Periodic Respiratory Health Evaluation Questionnaires	
	9. Physical Examination Form	
	10. Kansas Cancer Registry Validation Form	

Southeast Kansas Health Study

III. Narrative Statement

During public hearings in 1995 and 1996 on the permitting of Ash Grove Cement Company in Chanute, Kansas, residents expressed concern over the possible health effects of four hazardous waste combustors operating in the area. To respond to these concerns, the U.S. Environmental Protection Agency commissioned the University of Kansas Medical Center to conduct a health study to determine if environmental releases from hazardous waste burners and other industries in the cities of Chanute, Coffeyville, Fredonia, and Independence, Kansas, could be associated with health problems in these communities.

This document outlines the final protocol of a study to evaluate human health and air quality in these four communities and a control community of Sedan, Kansas, to ascertain whether or not an association exists between health problems in the communities and environmental factors. The study has three components: (1) a respiratory health survey and medical evaluation; (2) an epidemiological investigation of cancer incidence and mortality rates; and (3) an environmental assessment that includes the review of existing air monitoring data from the study communities, and the collection and analysis of ambient air samples from study and control communities over a one-year period during the study. (The detailed environmental monitoring assessment plan is attached to this document as Appendix A.)

The study's respiratory health component includes administering health questionnaires to randomly chosen households in the study and control communities. Based on the returned questionnaires as well as patient information collected from hospitals in the study and control communities on emergency room visits for acute respiratory illness, individuals who appear to be at elevated risk for adverse respiratory outcomes will be identified, and a sample group of approximately 250 individuals will be randomly selected to participate in a one-year respiratory health medical evaluation. Tally sheets also will be kept on inhaler use in schools in the study and control communities for a one-year period during the study. In the final phase of the study, all respiratory health data collected for the study and control communities will be compared, and environmental and medical data will be examined for associations between environmental factors and adverse respiratory outcomes.

The epidemiological investigation of cancer incidence and mortality rates builds upon an earlier preliminary epidemiological study of pediatric cancers in the area performed by the Kansas Department of Health and Environment. This follow-on study will evaluate cancer incidence and mortality rates in the study and control areas. Data for this portion of the study will be abstracted from the vital records section of the Kansas Department of Health and Environment, the Kansas Cancer Registry, and the National Cancer Institute's Surveillance, Epidemiology and End Result (SEER) program. The cancer incidence and mortality rates of the study and control counties will be compared and then examined in relation to environmental data on toxic agents of exposure in air to residents of the study areas. Data on cancer incidence and prevalence will also be obtained from a portion of the respiratory health questionnaire. Comparison will be made between exposed and control counties and communities. Investigators also will conduct literature reviews of these toxic agents to identify their level of risk with respect to causing cancer in humans.

IV. Study Background and Rationale

In Southeast Kansas, four commercial hazardous waste combustors (three cement kilns and an incinerator) operate within a 25-mile radius. According to the U.S. Environmental Protection Agency (EPA), this area supports the highest concentration of commercial hazardous waste burners in the country. The four operations are Ash Grove Cement Company in Chanute; APTUS/Laidlaw (recently renamed Safety-Kleen, Inc.) in Coffeyville; Lafarge Corporation in Fredonia; and Heartland Cement Company in Independence. Monarch Cement Company, also located within this 25-mile radius, has burned hazardous waste in the past, but now burns tires for fuel.

EPA and the Kansas Department of Health and Environment (KDHE) are responsible for permitting these hazardous waste operations. During public hearings held in 1995 and 1996 on the permitting of the Ash Grove Cement Company, area citizens expressed concerns to the EPA and the American Lung Association (ALA) that health problems in the community are related to stack emissions from combustion operations. Residents also expressed concern about releases of cement kiln dust into air and water, and waste generated by cement manufacturing. Some citizens requested that a health study be conducted, while others indicated that an extensive environmental monitoring program was required. EPA responded to the public's concerns by committing funds to conduct a health study of the four affected communities.

As stipulated by EPA, this study will focus on the towns of Chanute, Coffeyville, Fredonia, and Independence, Kansas. The study will have environmental and health effects components. The study's environmental component will evaluate the health implications of existing environmental data and identify environmental data gaps to be filled during the study. The study's health effects component will address respiratory health and cancer incidence and mortality rates in the study area. The cancer investigation will build upon an earlier preliminary epidemiological study of pediatric cancers in the area performed by KDHE. Investigators will identify and collect the necessary environmental and medical data to complete the study.

V. Applicant Background

The Center for Environmental and Occupational Health was established in 1985. It is dedicated to providing its clients with excellence in clinical and preventive medicine, and in educational and research programs directed at understanding the relationships between human health and hazards in the environment.

To fulfill its mission, the center draws on the expertise of a full-time staff that includes environmental and occupational medicine physicians, nurses, toxicologists, and an industrial hygienist. The center's 17 doctorally trained members devote all or a portion of their time to center activities. Members and staff combined offer specialized skills in the following research and technical areas: biochemical, clinical and industrial toxicology; clinical pharmacology; environmental chemistry; environmental medicine; epidemiology; industrial hygiene; metals analysis; occupational health; and risk assessment.

The center's program areas focus on a broad range of activities related to occupational and environmental health, laboratory services, and research and education.

Occupational and Environmental Health

The center's Department of Occupational Health and Environmental Medicine provides clinical occupational health services for the University of Kansas Medical Center, other Kansas state agencies, and clients in the community. The mission of the department is to provide employers with the medical services needed to maintain a healthy and safe work environment for their employees.

Services the department provides include preplacement examinations, OSHA-mandated medical surveillance examinations, program development for non-OSHA mandated surveillance in special workplace exposure situations, medical consultations for accident investigations, evaluation and treatment of work-related injuries and illnesses, and workers' compensation case management.

The department's medical staff consists of physicians educated in occupational medicine, nurse practitioners, occupational health nurses, and a nurse case manager. All personnel are dedicated to providing up-to-date occupational and environmental health needs based upon federal and state laws and current medical information. The department works closely with the other center divisions and departments at the University of Kansas Medical Center to provide quality customer service.

Environmental Health and Laboratory Services

The center's Field Services Division assists health-care providers, government and industrial agencies and patients/customers in understanding the health risks associated with exposure to toxic substances. The division offers customers a variety of environmental health services ranging from telephone consultations on possible toxic exposure problems to on-site monitoring, support and intervention services, including laboratory analyses, for large-scale occupational and environmental emergencies.

Research and Education

Center members are supported by federal and industrial grants. Members and staff conduct research in the areas of biochemical pharmacology, industrial hygiene, molecular biology, occupational medicine, epidemiology and toxicology.

As part of its mission, the center supports occupational and environmental education programs. Staff members serve as instructors for a variety of internal and external courses relating to industrial hygiene, environmental and occupational medicine, environmental health, environmental sampling and analysis, risk assessment, and environmental remediation.

Quality Assurance and Accreditation

Participating in quality assurance and accreditation programs is an important part of the center's activities. The Field Services Laboratory participates in quality assurance programs of the College of American Pathologists, the Centers for Disease Control and Prevention, the American Industrial Hygiene Association, and the Quebec Interlaboratory Comparison Program. It also is an OSHA-approved blood lead laboratory.

Collaborative Ties

The center maintains collaborative research and teaching programs in environmental and occupational medicine with the University of Kansas Medical Center's basic research and clinical departments, and with the University of Kansas Department of Civil & Environmental Engineering and the Center for Environmental Education and Training of the Continuing Education Division. The center also has active working relationships with the National Institute of Environmental Health Sciences, the National Institute for Occupational Safety and Health, the Department of the Navy, and the U.S. Environmental Protection Agency.

VI. Study Work Plan

A. Study Objectives

Key objectives of this study are as follows:

1. Perform a human health study in the southeast Kansas communities of Chanute, Coffeyville, Fredonia, and Independence focusing on the operation of four commercial hazardous waste burners in the area and other potential sources of environmental releases. The study has three components: (1) environmental data evaluation, and collection and analysis of ambient air samples during one study year; (2) a respiratory health survey and one-year respiratory health medical evaluation; and (3) an epidemiological investigation of cancer incidence and mortality rates. The cancer investigation builds upon an earlier preliminary epidemiological study of pediatric cancers in the area performed by the Kansas Department of Health and Environment.
2. Solicit stakeholder involvement in the design and performance of the study.
3. Communicate the results of the study to all stakeholders.

For the purposes of this study, stakeholders EPA has identified include but are not limited to citizens; local, state, and federal health officials; local physicians; local university researchers; local health and environmental advocacy groups; industry representatives; KDHE; and EPA.

B. Project Results/Benefits Expected

Project results and benefits that may be expected from the performance of the study include the following:

1. Stakeholders will learn whether or not health problems in the study area are associated with environmental factors.
2. Target groups within the study communities will receive free pulmonary function testing. Test results not only will provide key data for the study, but may also provide important early disease intervention information for some study participants.
3. Additional information may be acquired on the effects of combustion operations on human health.
4. Additional information will be accumulated on air quality in the study and control communities.
5. Research results may provide important health information to the study and control communities, as well as to future investigative studies, regulatory strategies, and medical intervention strategies.

6. Stakeholder and community meetings will create an environment that fosters open communication and trust between the various stakeholders.

C. Study Approach

1. Project Accomplishment

The study will be conducted in three phases. Phase I will be conducted from September 1, 1997 through January 14, 1999; phase II from January 15, 1999 through January 14, 2000; phase III from January 15, 2000 through September 30, 2000. The study's original start date was amended to September 1, 1997; its end date is stipulated as September 30, 2000.

Phase I - September 1, 1997 through January 14, 1999

Present Study's Draft Protocol at Stakeholder and Community Information Meetings in Chanute, Coffeyville, Fredonia, Independence, and Sedan

Phase I of the study has been devoted to presenting the draft protocol to stakeholders and residents at meetings held in the study communities and in Sedan, Kansas, the study's control community. Sedan was selected as the control community because it has its own hospital, it has no industries that produce environmental releases, and it is located upwind from the combustors in the study area.

Individuals who attended stakeholders meetings included mayors; city managers; city commissioners; local hospital representatives; chamber of commerce representatives; county health officers; representatives from Ash Grove Cement Company, APTUS/Laidlaw (recently renamed Safety-Kleen, Inc.), Lafarge Corporation, Heartland Cement Company, Farmland Industries, Kansas Department of Health and Environment, EPA, and ATSDR; investigators from KUMC; local physicians; representatives from local environmental and health advocacy groups; and the news media.

Informal community information meetings were held in each of the target communities and Sedan to present the study's draft protocol, to answer questions from residents, and to solicit comments on the proposed research plan. Members of the study team worked with the news media and city officials to set up these meetings. Before each meeting, press releases were sent to local radio stations, TV cable companies, and local and regional newspapers. The EPA paid for the rental cost of facilities where meetings were held.

Establish Advisory Committee

During phase I, investigators established an advisory committee that will be consulted at various points during the study. Members of the advisory committee include *ad hoc* member Dr. Ross Brownson, St. Louis University; Ms. Judy Keller, American Lung Association of Kansas; Dr. Dee Vernberg, The University of Kansas; Dr. Gary Spivey, Kansas Foundation for Medical Care; Dr. Jimmie Browning, Kansas Medical Society; Mr. Jan Sides, Kansas Department of Health and Environment; Cmdr. David Parker, Agency for Toxic Substances and Disease

Registry; and Ms. Natalie Storey, Burlington Northern Railroad. Ex-officio members of the committee include, Mr. John Smith, U.S. Environmental Protection Agency; Dr. H. William Barkman, KU Medical Center; Dr. John Neuberger, KU Medical Center; Dr. William Jewell, KU Medical Center; and Dr. Dennis Lane, The University of Kansas.

Review Existing Air Sampling Data

During phase I, investigators reviewed existing air sampling data from the study area. A review was conducted of other community industries that emit air pollutants. Based on information discussed at stakeholders and community information meetings, investigators have developed a detailed air sampling strategy for the study's sample collection year, projected to begin on or about January 15, 1999 and ending on or about January 14, 2000. The environmental monitoring plan is attached to this document as Appendix A.

Conduct Epidemiological Investigation of Cancer Incidence and Mortality in Study Area

One component of the health study builds upon an earlier preliminary epidemiological study performed by KDHE of pediatric cancers in the area. There are several phases to the investigation. They are summarized below.

Identification of toxins -The investigator will complete his review of existing data from industry and government sources concerning the toxic agents of exposure in air to residents in the study areas. Attention will be paid to the extent to which any of these agents exceed Federal standards or guidelines. Data from the environmental monitoring portion of the study will be used for determining toxins and specific amounts.

Literature Review - The investigator has conducted a literature review of these toxic agents and identified their level of risk with respect to causing cancer in humans (e.g., dioxin and PCBs). The investigator also has reviewed the literature concerning cancers among incinerator operators, cement kiln operators, fire department employees, and refinery workers. Other groups may be included if needed.

Case Finding - Cancers to be studied include all major cancer groups (25 for males, 28 for females). Of particular interest will be cancers possibly related to the exposures of concern. These include cancers of the brain, lung, skin, soft tissue sarcoma, non-Hodgkin's lymphoma, leukemia, and total (of these). For children aged 0-19, a similar grouping of cancers will be studied.

Cancer mortality data will be obtained from the vital records section of the Kansas Department of Health and Environment. Data for cancer rates from 1990 to 1997 will be obtained. If necessary, data for 1980-1989 will also be utilized in a supplementary analysis.

Population data will be obtained from the U.S. Census for 1990 (and 1980 if necessary). Data will be restricted to residents of Kansas and will be stratified into 18 age groups (0-4, 5-9, 10-14, ...75-79, 80-84, 85+). For pediatric cancers, four age strata will be used (0-4, 5-9, 10-14, 15-19). These data will be used to calculate the expected number of deaths from selected cancers in the

exposed towns and counties and in the appropriate control counties. Analysis will be race and sex specific and -- for pediatric cancers -- both sexes combined. A subset analysis will calculate the expected number of deaths in the exposed towns and counties using death rates from the nearby control counties.

Cancer incidence data will be obtained from the primary site reported to the Kansas Cancer Registry, University of Kansas Medical Center. The time period chosen for case finding and population count will be the latter ones used above. Data will be stratified by age groups, as above. Expected number of cases will be calculated as above. Analysis will be sex specific and sexes combined (pediatric cancers), as above. Because the cancer registry is not completely population based, a separate expected number of cases analysis will be run using cancer incidence data from the SEER (Surveillance, Epidemiology, and End Results) program of the National Cancer Institute. A third analysis will utilize the nearby control counties to generate the expected number of cases in the exposed towns and counties. Reports for 1997 from local hospitals and physicians in the exposed and nearby control counties will be sought concerning cancer in residents of the studied towns and counties. These cancer reports may be of assistance in ascertaining the degree of completeness of cancer reporting to the Registry. It is recognized that non-melanoma skin cancers are under-reported.

Data on the expected cancers (incidence and mortality) will be compared to cancers observed in the exposed and nearby control counties. The ratio of observed to expected cancers will be utilized as a measure of excess risk of cancer in both the exposed and the nearby control counties.

If more than one cancer is identified in a non-white, then an analysis will also be done for all races. This would involve the use of population, incidence, and mortality data for non-whites. If more than nine cancer cases in non-whites are identified, then the analysis will also include non-whites.

An additional source of cancer data will be obtained from the respiratory health questionnaires. The incidence and prevalence of cancer during the period 1990-1998 will be compared between the exposed and non-exposed groups. Analysis will be sex and race specific and could include whites, non-whites, and all races. Age group comparisons will be utilized.

An attempt will be made to have the State Health Department and the Kansas Cancer Registry spot map the cases of pediatric cancer in the exposed and non-exposed cities on geographically-based population density maps provided by EPA. Additional spot mapping of pediatric cancer cases will be done using residential information from the questionnaire. As with other spot mapping, after all the cases are carefully plotted, all identifying street location information will be removed.

Statistical Methods - Simple univariate analysis will be utilized to characterize the age, sex, county of residence, and date of diagnosis. Bivariate analysis will be utilized to characterize the risks by geographic location. For cancer incidence and mortality data obtained from pre-existing records, Standardized Mortality and Morbidity Ratios will be calculated and the method of Chiang will be used for calculation of statistical significance. For comparison of cancer

incidence and prevalence percentages obtained from the respiratory questionnaire, the method of Breslow and Day will be used for calculation of statistical significance. No statistical analysis of the pediatric cancer maps is planned at this time. Visualization of the results is planned.

Meetings - Meetings will be held with the health departments in all participating counties to seek suggestions and input. Community Health Assessment reports regarding cancer will be sought. The Kansas Department of Health and Environment will be contacted to discuss their work in pediatric cancers in this region. Any suggestions that they might have regarding this study will be sought.

Counties - Counties selected as exposed will be based on the environmental survey. However, to start with, Montgomery, Neosho, and Wilson counties will be selected. Nearby southeast Kansas non-exposed (control) counties will be Allen, Bourbon, Cherokee, Crawford, Chautauqua, Elk, Greenwood, Labette, and Woodson. This list of control counties will be refined further after examination of population and other data circa 1990. It is recognized that Cherokee county's lung cancer rate in white males is elevated due to cigarette smoking coupled with lead/zinc underground mining exposures (radon progeny and other particulates). Exposed towns will be Chanute, Coffeyville, Fredonia, and Independence. Non-exposed (control) towns will be obtained from the nearby control counties cited above.

Additional control cities and counties will be utilized. These will come from the state (Kansas) as a whole and from similar cities/counties ($\pm 50\%$ in population). The state of Iowa as a whole will also be utilized for incidence data only.

During phase I, exposed and non-exposed towns and counties will be selected, meetings will be held with public health agencies and townspeople, expected numbers of cancer cases will begin to be generated, and a start will be made both on the literature review and on obtaining the observed number of cancer cases in the exposed areas.

A sensitivity analysis will be performed to see what impact occurs when Cherokee County is removed as a control county for white male lung cancer deaths. A similar approach will be used for any control counties/cities with oil refineries.

A validity check will be performed for incidence data. A cover letter, pre-paid envelope, and a patient information form (sample attached to Appendix B of this document) will be mailed to hospitals and physicians in the area and in nearby treatment locales soliciting information on new cancer cases. All newly diagnosed cancer cases that are reported by physicians or hospitals for 1997 will be sent to a special mail box in the Department of Preventive Medicine; the material will be forwarded to the Kansas Cancer Registry unopened. The three exposed and one control county will be included as well as specialty hospitals elsewhere (e.g., Mayo Clinic, M.D. Anderson Cancer Center, and St. John's Regional Medical Center). Advertisements will be placed in local area newspapers encouraging area residents to contact their physicians to ensure that their cancers have been reported to the Registry. The validity check will be performed for 1997 only.

As a result of this activity, two separate rates will be calculated for each of the four counties; a completeness percentage and a reporting percentage. This will be done for all cancers, excluding non-melanoma skin cancers.

I. Completeness percentage = $\frac{\# \text{ cases in registry (of those below)}}{\# \text{ cases reported and confirmed}} \times 100$

II. Reporting percentage = $\frac{\# \text{ cases reported and confirmed}}{\# \text{ cases in registry (total)}} \times 100$

The study protocol to be used in the respiratory health and cancer components of the proposed study will be submitted to the Human Subject's Committee of the University of Kansas Medical Center for its approval. The questionnaire used in the respiratory health component will also be submitted for approval. Completed, returned questionnaires will be stored in locked files cabinets at KU Medical Center. Only study investigators will have access to the questionnaires. The confidentiality of all study participants will be preserved.

Develop and Disseminate Study's Final Protocol

The study's final protocol takes into consideration information discussed at stakeholders and community information meetings. The protocol includes the identification of researchers; a detailed budget; environmental and medical testing strategies (detailed in Appendix A and B); a communication strategy; and an estimate of the duration of the study. Copies of the final protocol will be sent to the advisory committee, stakeholders, and to local libraries in the study area.

The success of this study depends upon community involvement and cooperation in all phases of this investigation. During phase I of the study, investigators made 10 trips to the study area to meet with stakeholders and residents. The study team's environmental scientists made a number of other trips to the study communities to map the area, to identify sources of environmental releases, and to select sites for air samplers.

Stakeholders and residents of the study and control communities will be asked to review and comment on the final protocol in writing during a six-week period starting at the time the protocol is disseminated. At the end of that time, a community information meeting will be held in the study area to give residents and stakeholders an opportunity to ask questions and voice concerns about the study and related issues in a public forum. The decision on what becomes a part of the study's final protocol will be made by the study investigators.

Phase II - January 15, 1999 through January 14, 2000

Phase II of the study will be devoted to collecting the necessary environmental and medical data needed to complete the study.

Collect and Analyze Air Samples

During phase II, the study's environmental scientists will begin collecting ambient air samples at sampling sites in and around the communities of Chanute, Coffeyville, Fredonia, Independence, and Sedan, Kansas. The actual types of ambient air sampling and the frequency of each type of sampling have been determined during phase I of this project. These sampling decisions were based on the protocol discussed during stakeholder and community meetings. It is anticipated that the ambient air sampling effort will be intensive for a calendar year with extensive laboratory analysis of the samples during the actual sampling year and into the following year. Some additional ambient air sampling may be done in subsequent months after the formal year of sampling to fill in any data gaps that may exist in this area of the project. Actual sample types are whole air samples in Summa canister and PM10 and PM2.5 samples with mini-vols. The Environmental Monitoring Assessment Quality Assurance Project Plan attached as Appendix A to this document outlines in detail the methodology for air sample site selection, and sample collection and analysis.

Administer Health Questionnaire

During phase II, investigators will administer modified versions of the adult and children's standard American Thoracic Society (ATS) respiratory health questionnaires to randomly selected households in the study and control communities (attached to Appendix B of this document). The sample frame for the survey will be obtained by identifying each residential household in the five communities using county tax records. Each county office will provide us an electronic file with residential addresses for each parcel of residential property and each apartment that will be used to develop the sample frame. For the two smaller communities (Sedan and Fredonia), all households will be included in the sample for the questionnaire, thereby providing a complete census of households. For the three larger communities (Coffeyville, Independence, and Chanute), 2,500 households will be selected randomly from the sample frame of households in the community. The total number of households receiving a questionnaire is estimated to be 9,400.

The number 2,500 is based on the estimated number of households needed to identify 50 adult subjects for a respiratory health medical evaluation substudy, assuming a prevalence of sensitive subjects of 10 percent (we anticipate that the actual number is between 10 and 20 percent) and a questionnaire response rate of 20%. Assuming that we obtain at least 400 respondents from a community and the population prevalence is 15 percent or less for a particular condition, the 95% confidence interval for the population will be $\pm 3.5\%$ or less.

The survey instructions request that in each household surveyed one adult and one child (if present) complete and return questionnaires. To assure random sampling, responses will be requested from the adult and child with the most recent birthday. The primary analytic objective of the questionnaire is to obtain estimates of the prevalence of major respiratory illnesses in each of the participating communities and to compare prevalence in each of the combustor communities to that in the control community. The questionnaire will also supply a pool of subjects for the one-year respiratory health medical evaluation.

Collect and Review Hospital Data on Visits for Acute Respiratory Illness

Data on emergency room visits for respiratory illness, primarily asthma, bronchitis, acute shortness of breath, and exacerbations of chronic obstructive pulmonary disease will be obtained from hospitals in the study and control communities. Data will be collected from Neosho Memorial Hospital in Chanute, Fredonia Regional Hospital in Fredonia, Mercy Hospital in Independence, Coffeyville Regional Medical Center, and Sedan City Hospital in Sedan. The data will be collected for one year before the startup of hazardous waste combustion operations and one year after operations began (excluding the study's data collection year) in each community. (Ash Grove Cement Company in Chanute began burning hazardous wastes in 1988. Lafarge Corporation in Fredonia began burning hazardous waste in 1983 or earlier. Heartland Cement Company in Independence began burning hazardous waste in 1982 or earlier. Safety-Kleen, formerly known as Aptus/Laidlaw Environmental Services in Coffeyville began burning PCB's in 1986 and other hazardous waste in 1990.) During the study's data collection year, projected to begin on or about January 15, 1999 and to end on or about January 14, 2000, emergency room data will be abstracted monthly.

Data collected will include the following patient/case information: 1) name; 2) age; 3) gender; 4) patient's street address, town, and zip code; 5) date of visit; 6) treating hospital; a. admit or not; b. length of stay; or c. death; 7) diagnosis; 8) presence of existing respiratory disease and date of diagnosis; 9) cause of visit; a. medication noncompliance; b. infection; or c. environmental factors. Analysis of these data will allow investigators to compare respiratory outcomes between the study and control populations and with air quality data for the same time periods, if they are available. The data from hospital records also will be used to identify subjects for the respiratory health medical evaluation pool.

Inhaler Use in Study and Control Community Schools

Tally sheets monitoring student use of inhalers will be kept in each school in the study and control communities for a one-year period corresponding with the study's data collection year. Inhaler use will be monitored on a daily basis by either the school nurse or secretary. Sheets will be collected on a monthly basis by study staff. The information collected in the tally sheets will allow investigators to determine inhaler use rates in school children over the study's data collection year. In combination with environmental data, the inhaler information will be used to examine the relationship between air quality and respiratory outcomes in each of the study communities, and to assess whether those relationships vary by community.

Select Participants for One-Year Respiratory Health Medical Evaluation

Sample frames will be developed for each study and control community from returned and completed respiratory health questionnaires and hospital data collected on emergency room visits. The individuals to be included in sample frames will be adults, defined as 13 years of age or older. The health criteria for their inclusion are as follows: history of wheezing, asthma or emphysema. From the sample frames, 50 individuals will be randomly selected from each study and control community to participate in a one-year respiratory health medical evaluation corresponding with the study's data collection year.

Sample frames will be random ordered, and the top 50 individuals will be invited to participate in the respiratory health medical evaluation. If an individual declines to participate, then the next individual on the list will be contacted and invited to participate.

Take Health Histories, Conduct Physical Examinations, and Pulmonary Function Testing

During phase II, study participants will complete medical histories using an abbreviated form of the standard American Thoracic Society (ATS) health questionnaire (sample attached to Appendix B of this document); undergo a brief physical examination, including blood pressure check, and listening to the heart and lungs; and pulmonary function testing. Medical histories, physical examinations and pulmonary function testing will be performed in the KU Medical Center's mobile medical unit by a physician and a nurse practitioner. Respiratory health medical evaluations will be performed once at the beginning and end of the study's data collection year.

The information gathered from medical evaluations will give investigators a more detailed view of possible triggers of acute respiratory illness and the potential for excess loss of lung function. In the case of lung function measurements, predicted function is based upon age, gender, race and height. Examinations and lung function testing will validate diagnoses obtained from respiratory health questionnaires and medical histories, and will provide baselines for repeat examinations and pulmonary function testing during phase III of the study.

Conduct Epidemiological Investigation of Cancer Incidence and Mortality in Study Area

During phase II of the study, all case findings for the cancer component of the health study will be completed, additional literature reviews will be accomplished, and statistical analysis will be completed.

The duration of phase II is estimated to be one year, starting on or about January 15, 1999, and ending on or about January 14, 2000.

Phase III - January 15, 2000 through September 30, 2000

Take Health Histories and Conduct Physical Examinations and Pulmonary Function Tests

During phase III, study participants in the respiratory health medical evaluation will undergo a review of their medical histories, brief physical examinations, and pulmonary function testing. These activities will be conducted in the KU Medical Center's mobile medical unit under the supervision of a physician and a nurse practitioner. The medical data will be compared between study and control communities and with environmental data collected during the study's data collection year.

Analyze Data and Develop Study's Final Report

Phase III of the study will be devoted to analyzing data, preparing the study's final report and communicating study results to stakeholders and residents in the study and control communities.

Reports on cancer incidence and mortality rates in the study area will be made to all interested parties. Any recommendations for future research or medical and environmental intervention strategies will be made during this phase.

2. Facilities

The University of Kansas Medical Center

Facilities available at the University of Kansas Medical Center for use in carrying out this study include the following:

Mobile Medical Unit

The center's mobile medical unit is outfitted with two examining rooms and tables, phlebotomy capability, audiometry, mammography, X-ray, and pulmonary function equipment. The unit includes a refrigerator, bathroom, three wet sinks, heating and air conditioning. The unit travels throughout the region providing a variety of health-care services to urban and rural communities, and conducting research studies. It is ideally suited to conduct on-site health monitoring and surveillance tasks.

Field Services Division Laboratory

The Field Services Laboratory of the Center for Environmental and Occupational Health contains 790 ft² of space. Specialized equipment is used to analyze biological and environmental samples for heavy metals, including cadmium, chromium, copper, lead, mercury, nickel, and zinc, and other substances that have been identified as potentially harmful to human health. Data retrieval systems allow division staff to access software programs such as Micromedex's POISINDEX™, SilverPlatter's CISDOC, HSELINE, MHIDAS, HIOSHTIC, and OSH, and the HyperReader Electronic Pesticide Dictionary.

The center's laboratories contain state-of-the-art instrumentation, including gas and high-performance liquid chromatography, graphite tube atomic absorption and Fourier transform infrared spectroscopy, and potentiometric stripping analysis.

Library

The Archie Dykes Library at the University of Kansas Medical Center offers current health sciences information to support teaching, research, and clinical practice. The library contains approximately 57,500 monographs and 88,000 journal volumes. Journal subscriptions total about 1,600 titles; the subscription list is reviewed annually. Librarians are available to assist in locating information, in conducting research, in formulating research strategies, and in using library resources.

The library has access to several hundred databases and provides computerized searches of all the important health sciences databases. All library searchers are trained by the National Library

of Medicine and by one or more commercial database providers. Remote access is possible 24 hours a day through personal computers with modems.

Offices and Computers

All study investigators have private offices with computers. The center has 1,064 ft² of office space. Center staff have six personal computers and two Macintosh computers available to carry out word processing and data reduction tasks. Five of the six personal computers and one of the Macintosh computers are linked to the Internet.

The University of Kansas

Facilities available at the University of Kansas Main Campus, Lawrence, Kansas for use in carrying out the proposed study include the following:

Laboratory and Field Study Facilities

KU's Environmental Engineering & Science Laboratory includes over 10,000 ft² of space devoted to graduate student offices and both undergraduate and graduate teaching and research laboratories. Instrumentation is currently available to perform most analytical measurements usually associated with research investigations of water quality, air quality, and solid and hazardous wastes. Major equipment available for research includes: infrared, visible and ultraviolet spectrophotometers; two Perkin Elmer atomic absorption spectrophotometers; carbon, hydrogen, nitrogen and oxygen analyzers for solid materials; a Carlo Erba Carbon/Nitrogen Analyzer; a Dohrmann DC-80 TOC Analyzer with modules for purgeable organics and soil/sediment samples; a Dohrmann DX-2000 TOX Analyzer; three Varian gas chromatographs with ECD, FID, AFID, and TC detectors; three Hewlett-Packard gas chromatographs, including one with a cryogenic trap; a Shimadzu gas chromatograph with ECD and FID detectors; a Waters HPLC system; two Dionex ion chromatographs; Warburg respirometers; four controlled-environment rooms; four Zeiss research grade microscopes (including an epifluorescent microscope) and an Olympus microscope, all equipped with camera attachments; a Sorvall RC-5B Refrigerated Superspeed Centrifuge; and Applikon 3-L fermentor equipped with a Model ADI 1030 Bio Controller and a Model ADI 1012 Motor Controller; a Berglund-Liu vibrating orifice monodisperse aerosol generator; a TSI Submicron Particle Generator; a windtunnel for particle transport research; and an array of fast-response meteorological instruments; a Varian Saturn GC with a Varian mass spectrometer and cryogenic focusing capabilities. Several types of ambient air monitoring equipment which include: the VAPS (versatile ambient air sampling system; mini-vols (PM10 and PM2.5 inlets); whole air VOC samplers; and a wide range of specialized ambient air sampling systems for specific components.

Specialized research equipment is also available elsewhere on campus. Examples include high resolution mass spectrometers; scanning electron microscopes (including TEM and XRD capability and image analyzers), inductively coupled plasma spectrophotometers, an Alpkern RFA-300 continuous flow analyzer, an x-ray fluorescence spectrophotometer. The Engineering Microanalysis Laboratory (located in 1033A Learned Hall) houses a Phillips 515 scanning

electron microscope, EDAX PV-9900 energy dispersive spectrometer, Le Mont OASYS image analysis system, and Technics Hummer X Sputter coater. Frozen specimens can prepared for viewing using a Hexland CT 1000 Cryotrans System cold stage.

Computing Facilities

Excellent computing facilities are available both in Learned Hall and at the University Computation Center. The Engineering Computing Services facility is equipped with 12 Apollo DN4000 and 20 SUN workstations networked to the building Ethernet in Learned Hall. On the first floor of Learned Hall, there are two computer labs, one equipped with 30 486 PCS and one with 23 HP 286 PCS all networked to file servers. Another lab on the third floor contains 20 Macintosh Centris 610s, 5 Macintosh Centris 650s, and 5 Macintosh SEs. A well equipped second-floor computing facility is dedicated to use by graduated students in Civil Engineering (including EE&S students). Personal computers are available in faculty and student offices throughout the Civil Engineering Department and in the University Computation Center. Mainframe computers available on campus include an Amdahl 5890 (running MVS-XA); a DEC 7610 and 3 DEC 500s (running VMS-AXP); a DEC 500x and a DEC 500 running AXP-500s-OSF1; and two Model 350 IBM RS6000s running AIX.

Academic Computing Services provides a comprehensive campus fiber-based Ethernet communication system as well as an X.25 packet network. Users on the network can access all campus computing resources, resources in Kansas via KARENET, and resources around the world using MIDnet, INTERNET, and NSFNET.

Library Facilities

The library facilities at the University of Kansas provide excellent support for educational and research programs. Facilities include the Spahr Engineering Library located in Learned Hall, the new Science Library located nearby in Malott Hall, the Main Library (Watson), and a Government Documents Library. An exchange service also provides full access to the holdings of the Linda Hall Library in Kansas City and the library at Kansas State University. Computer-based literature searches can be conducted using terminals located in the Engineering Library and the Science Library, and an on-line catalog can be accessed through the campus network.

3. Non-federal Funding Sources and Facilities

This study will not use non-federal funding sources to help underwrite the cost of the project.

Non-federal facilities that investigators will use to conduct the study's stakeholders and community information meetings include high school or college auditoriums or gymnasiums in the study and control communities. These facilities will be reserved and rented through the EPA's Office of Public Affairs for Region VII.

4. Chronological Schedule of Project Accomplishments and Milestones

Task Phase I - September 1, 1997 through January 14, 1999	Year 1 Date Completed											
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
<ul style="list-style-type: none"> • Prepare Draft Study Protocol • Establish Advisory Committee • Conduct Stakeholders Meetings • Contact and meet with leaders of Sedan • Conduct Study and Control Community Information Meetings • Develop Health Questionnaire • Review Existing Air Sampling Data-ongoing • Select Study and Control Towns and Counties for Study's Cancer Component • Conduct Meetings with Health Officials and Town Residents for Study's Cancer Component • Conduct Literature Review for Study's Cancer Component • Obtain Observed Number of Cancer Cases in Exposed Areas for Study's Cancer Component • Finalize Statistical Design for Study's Environmental and Health Components 	6/30/97	8/31	12/15 12/15	1/13		3/2	4/7					
	6/30/97	11/30	Ongng 12/15	Ongng	Ongng	Ongng	Ongng	Ongng	Ongng	Ongng	Ongng	9/30
			12/15	1/13								
			12/31	Ongng	Ongng	3/31						
						Phase II						
											8/15	

Task Phase II - January 15, 1999 through January 14, 2000	Year 2 Date Completed											
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
<ul style="list-style-type: none"> •Complete and Disseminate Final Study Protocol • Hold Stakeholders Meeting on Final Protocol • Review Existing Hospital Data on Visits for Acute Respiratory Illness -Ongoing • Administer Health Questionnaire • Review Health Questionnaires • Select and Notify Study Participants • Take Health Histories, Conduct Physical Examinations and Pulmonary Function Tests • Collect and Analyze Air Samples - Ongoing • Collect and Analyze Data on Hospital Visits for Acute Respiratory Illness - Ongoing • Correlate Environmental and Health Data - Ongoing • Complete Literature Reviews for Study's Cancer Component • Collect Observed and Expected Number of Cancer Cases and Deaths 	10/9	11/18		X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
				X							X	

Task Phase III - January 15, 2000 through September 30, 2000	Year 3 Date Completed											
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
<ul style="list-style-type: none"> •Take Health Histories and Conduct Physical Examinations and Pulmonary Function Tests • Complete Statistical Analysis of Study's Environmental, Cancer, and Respiratory Health Components • Draft and Review Final Report • Complete Final Report • Hold Meetings with Stakeholders, and Study and Control Communities 								X	X			
								X	X	X		
										X	X	
											X	X

5. Indicate by whom each element of the work plan will be carried out including supporting agencies, consultants and contractors.

Staff	Role	Agency
<i>Health Effects Study</i>		
H. William Barkman, M.D.	Co-Prin. Investigator	University of Kansas Medical Center
John S. Neuberger, DrPH	Co-Prin. Investigator	University of Kansas Medical Center
J. Thomas Pierce, Ph.D.	Investigator	University of Kansas Medical Center
Dennis Wallace, Ph.D.	Investigator	University of Kansas Medical Center
William Jewell, M.D.	Consultant	University of Kansas Medical Center
Gregory A. Reed, Ph.D.	Quality Assurance Mgr.	University of Kansas Medical Center
Mary G. Walker, B.A.	Proj. Coordinator	University of Kansas Medical Center
Tom A. Anderson, M.S.	Driver/Eng.	University of Kansas Medical Center
Randall L. Brewer	Res. Assistant	University of Kansas Medical Center
Susan S. Lava, M.S.	Data Manager	University of Kansas Medical Center
To be Named	Nurse Practitioner	University of Kansas Medical Center
To be Named	HCA/Clerical	University of Kansas Medical Center
Mary Brothers, M.D.	MPH Student	University of Kansas Medical Center

Environmental Monitoring Study

Dennis D. Lane, Ph.D.	Co-Prin. Investigator	University of Kansas
Glen A. Marotz, Ph.D.	Investigator	University of Kansas
Richard W. Baldauf, M.S.	Investigator	University of Kansas
Ray E. Carter, Jr., M.S.	Investigator	University of Kansas

Phase I - September 1, 1997 through January 14, 1999

- *Prepare Final Study Protocol*

Drs. Barkman, Lane, Marotz, Neuberger, Wallace, Messrs. Baldauf and Carter, and Ms. Walker.

- *Establish Advisory Committee*

Drs. Barkman, Neuberger, Pierce, Lane, and Marotz.

- *Contact and Meet with Leaders of Sedan*

Drs. Barkman, Neuberger, Lane, Pierce, and Wallace; Messrs. Baldauf and Carter, and Ms. Walker.

- *Coordinate and Conduct Stakeholders and Community Information Meetings*

Drs. Barkman, Brothers, Neuberger, Lane, Pierce, Messrs. Baldauf and Carter, Ms. Cote, and Ms. Walker.

- *Develop Health Questionnaire*

Drs. Barkman and Wallace.

- *Review Existing Air Sampling Data*

Drs. Lane and Marotz, and Messrs. Richard Baldauf and Ray Carter.

- *Select Study and Control Communities and Counties for Study's Cancer Component*

Drs. Neuberger and Brothers

• *Conduct Meetings with Health Officials and Community Residents for Study's Cancer Incidence Component*

Drs. Neuberger and Brothers.

- *Conduct Literature Review for Study's Cancer Component*

Dr. Brothers.

- *Obtain Observed Number of Cancer Cases in Exposed Areas for Study's Cancer Component*

Drs. Neuberger and Brothers.

- *Finalize Statistical Design for Study's Environmental and Health Components*

Drs. Barkman, Wallace, Lane, and Marotz.

- *Complete and Disseminate Study's Final Protocol*

Drs. Barkman, Neuberger, Lane, Wallace, Mr. Baldauf, and Ms. Walker.

Phase II - January 15, 1999 through January 14, 2000

- *Collect and Analyze Air Samples*

Drs. Lane, Marotz, and Messrs. Baldauf and Carter.

- *Collect and Analyze Existing Hospital Data on Visits for Acute Respiratory Illness*

Drs. Barkman and Wallace, Ms. Lava, and Mr. Brewer.

- *Administer Health Questionnaire*

Questionnaire will be administered by mail. This task will be organized and executed by Ms. Walker and Mr. Brewer.

- *Review Health Questionnaires*

Drs. Barkman and Wallace.

- *Select and Notify Study Participants*

Dr. Barkman, Mr. Brewer, and Ms. Walker.

- *Take Health Histories and Conduct Physical Examinations and Pulmonary Function Tests*

Dr. Barkman, nurse practitioner and a clerical person.

- *Collect and Analyze Data on Hospital Visits for Acute Respiratory Illness*

Drs. Barkman and Wallace, Ms. Lava, and Mr. Brewer.

- *Complete Case Findings for Study's Cancer Component*

Drs. Neuberger and Brothers.

- *Complete Literature Reviews for Study's Cancer Component*

Drs. Neuberger and Brothers.

- *Complete Statistical Analysis for Study's Cancer Component*

Drs. Neuberger, Wallace, and Ms. Lava.

Phase III - January 15, 2000 through September 30, 2000

- *Take Health Histories and Conduct Physical Examinations and Pulmonary Functions Tests*

Dr. Barkman, nurse practitioner and the clerical person.

- *Correlate Environmental and Health Data*

Drs. Barkman, Wallace, Neuberger, Lane, Marotz and Mr. Baldauf.

- *Complete Statistical Analysis of Study's Environmental and Respiratory Health Components*

Drs. Barkman, Wallace, Lane, Marotz, Mr. Baldauf and Ms. Lava.

- *Draft and Review Final Report*

Drs. Barkman, Wallace, Neuberger, Pierce, Lane, Marotz, Mr. Baldauf, Ms. Lava, Ms. Walker.

- *Complete Final Report*

Drs. Barkman, Wallace, Neuberger, Pierce, Lane, Marotz, Mr. Baldauf, Ms. Lava, and Ms. Walker.

- *Hold Stakeholders and Communities Information Meetings on Study Results*

Drs. Barkman, Neuberger, Pierce, Lane, Marotz, and EPA.

6. Describe sampling and data collection procedures, analytical methods, and methods for evaluating the results and successes of the project.

Environmental Data Collection, Analysis, and Results Evaluation

The sampling frame design for air quality data will permit periodic and discrete sample collection at fixed and designated points within the study and control communities. All air samples will be collected by the study's environmental scientists using standard protocols. Analytical methods will include gas chromatographic, mass spectrometric, gravimetric, atomic absorption spectrophotometric and inductively-coupled plasma spectroscopic analysis. Inferential parametrical and nonparametrical procedures will be used to test relevant hypotheses. The sampling frame will also be used to collect meteorological information relevant to the selected air quality species at designated locations. The Environmental Monitoring Assessment Quality Assurance Project Plan, outlining the methodology for all air sampling collection and analysis, is attached as Appendix A to this document.

Epidemiological Data Collection, Analysis, and Results Evaluation of the Study's Cancer Component

Cancer incidence and mortality rates will be developed from the Kansas Cancer Registry and the Kansas Department of Health and Environment. In addition, cancer incidence data will be used from the National Cancer Institute's Surveillance, Epidemiology and End Result (SEER) program. Data on expected cancers will be compared with the study and control counties. Additional data will be obtained for 1997 from area physicians and hospitals. Additional data will be obtained on cancer incidence and prevalence among the population sample used for the respiratory health questionnaire.

Data Collection, Analysis, and Results Evaluation of the Study's Respiratory Health Component

Data Collection and Management

The respiratory health component of this study involves the collection of four primary data streams—questionnaire data received from the household survey, medical data on acute respiratory events obtained from hospital medical records review, data on inhaler use collected from schools in the participating cities, and medical data obtained from two medical examinations on each of the 50 subjects in each community participating in the one-year respiratory health medical evaluation. All data from each stream will be collected using an appropriate data collection form and entered into an electronic data base.

The data entry and data management system will be designed using Microsoft Access[®]. For each data stream, 15% of the records will be double entered. If greater than 0.1 percent errors in coding are found in any form, all forms will be double entered and compared with corrections made before the data are considered ready for analysis. After data entry and review are completed, the data will be converted to the SAS data system for analysis. A set of consistency and range checks will be run and all data reviewed before analysis is initiated.

Statistical Analyses

The primary analytic objective of the respiratory health questionnaire is to obtain estimates of the prevalence of major respiratory illnesses in each of the participating communities and to compare prevalence in each of the combustor communities to that in the control community. Because the data will be collected using a population-based survey instrument, point and interval estimates of population prevalence for each primary respiratory condition will be developed using appropriate sample weights. Weighted least squares techniques that are analogous to ANOVA techniques for continuous outcomes will be used to test for differences in prevalence among the study communities.

Data on use of inhalers in the schools and acute respiratory events based on hospital emergency room use will be collected on a daily basis throughout the year. These data will be used to

examine the relationship between air quality and respiratory outcomes in each of the study communities and to assess whether those relationships vary by community.

As part of the initial descriptive analyses, we will examine the year-long temporal patterns in respiratory events and air quality measurements at the different sites in the five communities to identify patterns that suggest possible relationships. As a part of these initial analyses, we will examine patterns of events as a function of both season and day of the week to assess whether those variables should play a role in subsequent analyses. Also these initial analyses will address whether data provide sufficient stability to examine events on a daily basis or whether aggregation across full weeks appears more reasonable.

After the descriptive analyses are completed, formal model based analyses using extensions of generalized linear models (McCullagh and Nelder, 1989; and Diggle, Liang, and Zeger, 1994) that account for the correlation imbedded in the repeated observations from the same communities will be used to assess the relationship of events to air quality. Again, depending on the numbers of outcomes for any particular unit of analysis, we will use either an identity link (if data appear to be normally distributed) or log link (if data behave as Poisson counts). Statistical inferences about the effect of air quality on respiratory events will be based on Wald-type tests using the robust variance estimator described by Liang and Zeger, 1986.

The primary outcome from the respiratory health medical evaluations will be the change in lung function over the course of the year. Level of lung function will be determined by predicted values based on age, gender, height, and race. The initial individual health evaluation will serve as the baseline for the follow-up evaluation that will occur at the end of the study's data collection phase. Thus, the individual will serve as his/her own control over the sampling period. Depending on the distributional properties of these change scores, either ANOVA models or the non-parametric Kruskal-Wallis analogue will be used to assess differences in change scores in the five communities.

D. General Program/Project Information

1. Identify the kinds of data to be collected (and maintained) and discuss the criteria to be used to evaluate the results and successes of the project.

Environmental Data

The atmospheric air quality constituents measured will include particulate matter, aerosols and gases. Specific species and constituents are identified in the environmental sampling plan attached to this document as Appendix A. Meteorological data also will be collected during the study period and will include measurements of temperature, relative humidity, wind speed, wind direction, and pressure. Synoptical weather conditions will be identified from standard weather charts. All atmospheric concentration and meteorological data will be archived electronically for public access. Conclusions reached will be based upon results from the analytical data, and the outcome of statistical testing procedures.

Epidemiological Data for Study's Cancer Component

With respect to the cancer component of the study, most of the cancer incidence and all of the cancer mortality data will be obtained from the Kansas Cancer Registry and KDHE (respectively). Comparison will be made between study and control counties. Depending upon the findings of the environmental data survey and the final protocol development, investigators may attempt to seek associations with specific environmental agents. Primary data collection will come from asking physicians and hospitals to report cases for 1997. An additional comparison for cancer incidence and a separate comparison for cancer prevalence will be obtained from the respiratory health questionnaire.

Respiratory Health Data from Study and Control Community Hospitals and Study Participants

Data on emergency room visits for respiratory illness, primarily asthma, bronchitis, acute shortness of breath, and exacerbations of chronic obstructive pulmonary disease will be obtained from hospitals in the study and control communities. Data collected will include the following patient/case information: 1) name; 2) age; 3) gender; 4) patient's street address, town and zip code; 5) date of visit; 6) treating hospital; a. admit or not; b. length of stay; or c. death; 7) diagnosis; 8) presence of existing respiratory disease and date of diagnosis; 9) cause of visit; a. medication noncompliance; b. infection; or c. environmental factors. The data will be collected for one year before the startup of hazardous waste combustion operations and one year after operations began in each community. During the study's data collection year, projected to begin on or about January 15, 1999 and to end on or about January 14, 2000, emergency room data will be abstracted monthly.

During the data collection year, tally sheets will be kept by all schools in the study and control communities on daily inhaler use by school children. The sheets will be collected on a monthly basis by project staff and entered into an electronic database. These data will be used to examine the relationship between air quality and respiratory outcomes in each of the study communities and to assess whether those relationships vary by community.

Modified versions of the adult and children's American Thoracic Society's standard respiratory health questionnaires (samples attached to Appendix B of this document) will be used to collect

information from adults and children in randomly selected households in the study and control communities. The questionnaires will allow investigators to obtain estimates of the prevalence of major respiratory illnesses in each of the participating communities and to compare prevalence in each of the combustor communities to that in the control community.

During the respiratory health medical evaluation, 250 participants from the study and control communities will complete a health history, using an abbreviated form of the American Thoracic Society's standard respiratory health questionnaire (sample attached to Appendix B of this document) and undergo a brief physical examination (including blood pressure check, and listening to the heart and lungs) and pulmonary function testing. The medical evaluation will occur once at the beginning of the data collection year and again at the end of the year.

Data collected during respiratory health medical evaluation of study participants will allow investigators to look in detail at a smaller group of people to determine the frequency of respiratory symptoms and severity of lung function abnormalities and potential changes in lung function over the study period. From this information Investigators will attempt to find an association with environmental data to determine if any of these pulmonary function changes can be attributed to environmental factors.

2. The effect of this program/project on, or its relationship to, other work planned, anticipated, or underway by the applicant, recipient of funds, or other government agencies.

The University of Kansas Medical Center and the University of Kansas are not currently conducting any similar environmental health studies in partnership with other federal, state, or industrial agencies.

3. Federal, state, interstate and local programs with which the work will be coordinated and the extent and nature of the coordination.

This study is being coordinated with the Kansas Department of Health and Environment, the American Lung Association of Kansas, the Environmental Protection Agency, and the Neosho, Montgomery, Wilson, and Chautauqua County Health Departments.

E. Itemized Budget

(See budget slides in Appendix 1 of the Final Report)

F. Human Subjects Protocol

In accordance with DHHS's regulations on Protection of Human Subjects (*45 CFR 46* as amended), The University of Kansas Medical Center has established a Human Subjects Committee to review all grants and projects involving human subjects. Members of this committee are Dr. Jerry Menikoff, Chairman; Dr. William G. Bartholome, Vice Chairman; Dr. Harold N. Godwin; Ms. Margaret Barnett; Dr. John M. Belmont; Ms. Beverly Bubeck, Dr. Timothy P. Daaleman; Dr. Paul A. DeCarolis; Dr. Kottarappat Dileepan; Dr. Chukuka S.

Enwemeka; Dr. Jameson Forster; Dr. Raymond Lake; Dr. Joan McDowd; Dr. Rajesh Pahwa; Mr. Steven L. Ruddick, Ms. Ruth Schukman-Dakotas; Dr. Margaret L. Smith; The Reverend Jerry Spencer; Dr. Daniel L. Stewart; Dr. Roma Lee Taunton; and Dr. Kathryn Veal.

Purpose of Research

The purpose of this research is to determine whether or not an association exists between health problems occurring in the communities of Chanute, Coffeyville, Fredonia, and Independence, Kansas, and the operation of hazardous waste burners and other emissions sources in those communities. The U.S. Environmental Protection Agency (EPA) commissioned the study in response to health concerns citizens raised at public hearings held in 1995 and 1996 during the permitting process of the Ash Grove Cement Company located in Chanute, Kansas. If results from this study indicate that an association exists between health problems in the area and environmental factors, EPA has indicated it “may perform additional evaluations of appropriate and effective regulatory actions to address these environmental factors.”

The study’s control community (Sedan, Kansas) was selected because it is located upwind from the research area and does not have industries producing environmental emissions.

Research Components

EPA requested that the grant’s research design include environmental data collection and evaluation, and a health effects study. The environmental component of the study involves the review of existing air sampling data collected in the study area, and the collection and analysis of ambient air samples from the area for a one-year period during the performance of the grant. This component does not involve the use of human subjects or the collection of human health data. A quality assurance project plan that includes a detailed protocol of the environmental component is attached to this document as Appendix A.

EPA specified that this study include a health effects component building on an earlier epidemiological study of pediatric cancers performed in the area by the Kansas Department of Health and Environment. Because many respiratory illnesses are induced or exacerbated by the presence and/or high levels of certain chemicals and particulates in the air, it was determined that a respiratory health component should be included in the study.

The research protocol outlined under the respiratory health and cancer incidence and mortality rates components of this study includes the use of human subjects and the collection of human health data. The human subjects aspects of these two components are addressed below.

Respiratory Health Study

The protocol for the respiratory health study includes the following key activities: 1) collecting patient information on emergency room visits for acute respiratory illnesses from hospitals located in the study and control communities; 2) administering a respiratory health survey to households randomly selected in each study and control community; 3) randomly selecting 50 individuals from each community to participate in a one-year respiratory health medical evaluation; and 4) collecting information on inhaler use in schools in the research and control communities during a one-year period. The protocol for the respiratory health medical evaluation includes completing a health history, undergoing a limited physical examination (including checking blood pressure and listening to the heart and lungs) and conducting pulmonary function testing. The respiratory health evaluation will be carried out twice--once at the beginning and once at the end of the study's data collection year.

Collecting Patient Data from Hospitals

Investigators will collect data on the number of emergency room visits to hospitals located in the study and control communities for respiratory illness, including asthma, bronchitis, acute shortness of breath, and exacerbations of COPD. The data collected will include the following patient/case information: 1) name; 2) age; 3) gender; 4) diagnosis; 5) date of event; 6) treating hospital; a. admit or not; b. length of stay; or c. death; 7) patient's street address, town, and zip code; 8) presence of existing respiratory disease; 9) date of diagnosis; 10) cause of event; a. medication noncompliance; b. infection; or c. environmental factors. Investigators will review hospital records for the year before hazardous waste combustion operations began in each study community, in one subsequent year after hazardous waste combustion operations began (excluding the data collection year), and again during the study's data collection year.

Patient data collected from hospitals will be used in several ways: 1) to develop a database on the incidence and suspected causes of acute respiratory events in the study and control populations; 2) in combination with information from the respiratory health questionnaires, to develop a sampling frame from which 250 study participants will be randomly selected to participate in a one-year respiratory health evaluation; 3) to examine the relationship between air quality and respiratory outcomes in each of the study communities; and (4) to assess whether those relationships vary by community.

Using a laptop computer, project staff will collect and enter hospital data directly into a Microsoft Access database designed for the study. All hospital data will be kept confidential and stored in locked file cabinets at the University of Kansas Medical Center. Only researchers involved in this study will have access to the data collected from hospitals. Any data published from this study will not include personal identifiers.

Administering the Respiratory Health Survey

Modified versions of the adult and children's American Thoracic Society standard epidemiologic respiratory health questionnaires (ATS-DLD-78-A and ATS-DLD-78-C) will be mailed to

single- and multiple-family dwelling units randomly selected in the study and control communities (samples attached to Appendix B of this document). County tax records will be used to develop the list of households to receive the questionnaires.

Each household selected to participate in the survey will receive an envelope containing a letter of information, an instruction sheet, an adult consent form, a parental permission form and child's assent form, two questionnaires (one for an adult and one for a child), and a postage paid return envelope. Copies of the consent forms and questionnaires are attached to the quality assurance project plan for the respiratory health and cancer incidence and mortality rates components of the study (Appendix B)

In each household, the adult and child (if present) who have had the most recent birthdays will be asked to complete questionnaires.

The information collected in these questionnaires will be developed into a database that will be used in the following ways: 1) It will be combined with patient data collected from hospitals in the study and control communities to produce a sampling frame for the selection of 250 participants for the respiratory health evaluation; 2) It will be used to generate information on the prevalence of respiratory illness in the study and control communities.

Selecting the Subject Population

The sample frame for the study's respiratory health survey will be obtained by identifying each residential household in the five communities using county tax records. Each county office will provide us an electronic file with residential addresses for each parcel of residential property and each apartment that will be used to develop the sample frame. For the two smaller communities (Sedan and Fredonia), all households will be included in the sample frame for the questionnaire. For the three larger communities (Coffeyville, Independence, and Chanute), 2,500 households will be selected randomly from all households in the community. The number 2,500 is based on the estimated number of households needed to identify 50 adult subjects for the substudy, assuming a prevalence of sensitive subjects of 10 percent (we anticipate that the actual number is between 10 and 20 percent) and a questionnaire response rate of 20%. Assuming that we obtain at least 400 respondents from a community and the population prevalence is 15 percent or less for a particular condition, the 95% confidence interval for the population will be $\pm 3.5\%$ or less. We recognize that this process may exclude a few households in each community because tax record data are incomplete or inaccurate. However, this approach will provide a nearly complete sample frame within the resource constraints of this study.

The 250 participants for the one-year respiratory health medical evaluation will be randomly selected from sample frames developed for each community from returned, completed questionnaires and patient data abstracted from study and control community hospitals for previous years. Individuals to be included in sample frames will be adults, defined as 13 years of age or older. The health criteria for their inclusion are as follows: history of wheezing, asthma, or emphysema. From each sample frame, 50 individuals will be randomly selected to participate in the one-year medical evaluation corresponding with the study's data collection year. Sample

frames will be random ordered, and the top 50 individuals will be invited to participate in the respiratory health medical evaluation. If an individual declines to participate, then the next individual on the list be contacted and invited to participate.

Conducting the Respiratory Health Evaluation

Study participants will complete medical histories using an abbreviated version of the standard American Thoracic Society (ATS) health questionnaire (sample attached to Appendix B of this document); undergo a brief physical examination (including blood pressure check, and listening to the heart and lungs); and undergo pulmonary function testing. Medical histories, physical examinations and pulmonary function testing will be performed in the KU Medical Center's mobile medical unit by a physician and a nurse practitioner. Examinations and lung function testing will validate diagnoses obtained from respiratory health questionnaires and medical histories, and will provide baseline information for repeat examinations and pulmonary function testing conducted at the end of the data collection year. Medical evaluations will be performed at the beginning and end of the study's data collection year.

Monitoring Inhaler Use in Study and Control Community Schools

Tally sheets monitoring student use of inhalers will be kept in each school in the study and control communities for a one-year period corresponding with the study year. Inhaler use will be monitored on a daily basis by either the school nurse or secretary. Sheets will be collected on a monthly basis by study staff. The information collected in the tally sheets will allow investigators to determine inhaler use rates in school children over the study's data collection year, to examine the relationship between air quality and respiratory outcomes in each of the study communities, and to assess whether those relationships vary by community. Since tally sheets collected for this study will not include the names of students, informed consent is not be required.

Risks versus Benefits of Research

Use and Storage of Health Information

Since all personal health information contained in questionnaires and hospital databases will be used only by investigators (on a need-to-know basis) for the performance of research tasks, no measurable risks are associated with this study. When not being used by researchers, questionnaires and databases will be stored in locked file cabinets at the University of Kansas Medical Center. Any data published from this study will not include personal identifiers.

Pulmonary Function Testing

A slight risk exists that a few participants in the respiratory health medical evaluation may experience very slight dizziness during pulmonary function testing. A physician will be present during testing to monitor the well being of all participants.

Benefits of Research

The benefits that study participants and communities will accrue from the research include the following: a) residents in the study communities will learn whether or not health problems in the study area are associated with environmental factors; b) study participants will receive free pulmonary function testing, which will provide key data for the study and may also provide important early disease intervention information to some participants; c) additional information may be acquired on the effects of combustion operations on human health; d) additional information will be accumulated on air quality in the study and control communities; e) results from the respiratory health survey and cancer incidence and mortality rates investigation will give study and control communities an idea of the prevalence of some respiratory illnesses and cancers in their communities; and f) tally sheets on inhaler use in schools will give residents an idea of the prevalence of respiratory problems among school children.

Processing the Research Data

The detailed discussion of how research data will be processed for this study is outlined under item 6 on pages 27, 28, and 29.

Monitoring

The data entry system is being designed with appropriate range and logic checks to limit inaccuracies in data entry, and routine data reports that document data quality will be generated. The study's quality assurance manager will be responsible for monitoring data quality and accuracy at regular intervals throughout the study.

Informed Consent Process

Informed consent forms have been developed for adults and children who participate in the respiratory health survey and for participants in the one-year respiratory health medical evaluation. Adults and children filling out the questionnaires will be asked to read, sign and return the appropriate consent forms with the completed questionnaires. Participants in the one-year medical evaluation will be asked to read and sign a consent form at the time they have their medical histories taken. Samples of informed consent forms, parental permission, and child's assent forms are attached to the quality assurance project plan for the respiratory health and cancer incidence and mortality rates components of the study (Appendix B).

Epidemiological Investigation of Cancer Incidence and Mortality Rates

Sources for most of the data used in the cancer incidence and mortality rates investigation will come from the existing publicly available databases of the Kansas Cancer Registry, the National Cancer Institute's Surveillance, Epidemiology, and End Results program, and the Kansas Department of Health and Environment.

An additional source of cancer data will come from the respiratory health questionnaires. This information will be protected by the informed consent forms prepared for the respiratory health component of this study. All data collected from the questionnaires and respiratory health medical evaluation will be used only by researchers on a need-to-know basis and will be stored in locked file cabinets in the University of Kansas Medical Center.

An attempt will be made to have the State Health Department and the Kansas Cancer Registry spot map the cases of pediatric cancer in the exposed and non-exposed cities on geographically-based population density maps provided by EPA. Additional spot mapping of pediatric cancer cases will be done using residential information from the questionnaire. As with other spot mapping, after all the cases are carefully plotted, all identifying street location information will be removed.

A validity check will be performed for incidence data. A cover letter, pre-paid envelope, and a patient information form (sample attached to Appendix B of this document) will be mailed to hospitals and physicians in the area and in nearby treatment locales soliciting information on new cancer cases. All newly diagnosed cancer cases that are reported by physicians or hospitals for 1997 will be sent to a special mail box in the Department of Preventive Medicine at KU Medical Center; the material will be forwarded to the Kansas Cancer Registry unopened. The three exposed and one control county will be included as well as specialty hospitals elsewhere (e.g., Mayo Clinic, M.D. Anderson Cancer Center, and St. John's Regional Medical Center). Advertisements will be placed in local newspapers encouraging area residents to contact their physicians to ensure that their cancers have been reported to the Registry. The validity check will be performed for 1997 only. All data collected for the validity check will be stored in locked files under the auspices of the Kansas Cancer Registry for five years and then destroyed.

G. Quality Assurance Requirements

Detailed Quality Assurance Project Plans for the environmental and health components of this study were included in the original copies of the study protocol delivered to study community public libraries and are available in the reference section of those libraries.

H. Biographical Sketch of the Project Manager - H. William Barkman, M.D.

H. William Barkman, M.D., M.S.P.H.
Director
Center for Environmental and Occupational Health
The University of Kansas Medical Center

EDUCATION

M.D., Creighton University, Omaha, Nebraska, 1974
M.S.P.H., Public Health, University of Utah, Salt Lake City, Utah, 1980
B.A., Chemistry, Drake University, des Moines, Iowa, 1969

SUMMARY OF PROFESSIONAL EXPERIENCE

1974-1975 Internship, Creighton University, Omaha, Nebraska
1975-1977 Residency, Internal Medicine, University of Oklahoma, Oklahoma City, Oklahoma
1977-1980 Fellowship, Pulmonary Diseases, University of Utah, Salt Lake City, Utah
1978-1980 Residency, Occupational Medicine, University of Utah
1978-1980 Physician, Respiratory Clinic, Carbon County Hospital, Price, Utah
1980 Instructor of Medicine, Department of Internal Medicine, University of Utah
1980 Staff Physician, Salt Lake City Veterans Administration Medical Center
1980-1985 Assistant Professor of Medicine, Dept. Internal Medicine, Tulane University, New Orleans, Louisiana
1980-1985 Associate Director, ICU, Charity Hospital of Louisiana, New Orleans
1982-1989 Director, Pulmonary Functional Laboratory, Tulane Medical Center
1982-1989 Co-Director, Respiratory Therapy, Tulane Medical Center
1983-1989 Director, Critical Care Medicine Program, Internal Medicine, Tulane Medical Center
1983-1989 Staff Physician, Veterans Administration Medical Center, New Orleans, Louisiana
1984-1989 Co-Director, Pulmonary Diseases Section, Dept. of Medicine, Tulane Medical Center
1985-1989 Associate Professor of Medicine, Pulmonary Diseases Section, Tulane Medical Center
1985-1989 Co-Director, ICU, Charity Hospital Louisiana
1986-1989 Director, Pulmonary/Critical Care Fellowship Program, Tulane University
1987-1989 Director, Intermediate Care Unit, Tulane Medical Center
1989-present Associate Professor of Internal and Preventive Medicine, University of Kansas Medical Center, Kansas City, Kansas
1989-1991 Assoc. Director, Center for Environmental & Occupational Health, University of Kansas Medical Center
1991-present Senior Physician, Center for Environmental & Occupational Health, University of Kansas Medical Center
1991-present Director, Center for Environmental & Occupational Health, University of Kansas Medical Center
1995-present Director, Johnson County, Kansas, Health Department Laboratories Services

- 1996-present President, Kansas Thoracic Society, Medical Section of the American Lung Association
- 1998-present Chief of Staff, University of Kansas Hospital, University of Kansas Medical Center

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