

**Appendix 4**

**Final Protocol Comments by Schreiber & Yonley Assoc.**

COMMENTS ON  
*SOUTHEAST KANSAS HEALTH STUDY*  
*FINAL PROTOCOL*

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On behalf of the  
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The Kansas Health Study Group has reviewed the *Southeast Kansas Health Study, Final Protocol* and wishes to provide preliminary comments on the study plans. The Kansas Health Study Group consists of representatives of the three cement plants in southeast Kansas that burn hazardous waste as supplemental fuel. The Kansas Health Study Group appreciates the opportunity to provide comments on the protocol, and anticipates providing continuous input into the health study as it proceeds. We believe that the study results will indicate that the operations of the cement plants in southeast Kansas do not adversely affect public health.

Since the document is stamped "Draft" and presents both a protocol and the quality assurance project plan for the performance of the study, we refer to it in this review as the "draft protocol".

**GENERAL COMMENTS**

**Study Objective**

The stated objective of the Southeast Kansas Health Study is identified in Section III of the protocol as "... to ascertain whether or not an association exists between health problems in the communities and environmental factors." Throughout subsequent portions of the draft protocol, this objective is abbreviated to determining whether there is an association of adverse health effects in the study communities only with the burning of hazardous waste. The abbreviated study objective consistently focuses on linking the burning of hazardous waste with adverse health effects in the four study communities.

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<sup>1</sup> The Kansas Health Study Group includes Ash Grove Cement Co., Chanute, Kansas; Heartland Cement Co., Independence, Kansas; and Lafarge Corporation, Fredonia, Kansas

The abbreviated objective that is presented throughout the protocol can appear misleading to the study stakeholders, and should be corrected throughout the text. As described below, because of limitations in the study design, we believe that the stated objective of the study cannot be met and that it should be redefined. This conclusion is based on deficiencies in several areas of the study, including:

- Population sizes
- Selection of the control community
- Method of selecting respiratory study objectives
- Adequacy and frequency of health measurements
- Adequacy of data collection methods for hospitalizations
- Statistical analytical method
- Population stratification.

These deficiencies are described in more detail in the specific comments that follow. The conclusion of the comments is that the study design deficiencies will result in a low statistical power of the study. As a result, study design, the study findings may not be valid or conclusive with respect to an association of health effects with sources of pollutant emissions, including the burning of hazardous waste. Therefore, the study design will not meet the objective stated in the draft protocol.

It appears that the KUMC representatives recognize the limitations in the study design. During a presentation on 17 October 1997, the KUMC representatives indicated that the study results will not be able to link any potential findings from the health survey with sources of emissions. Instead, the study objective was restated to provide information that could be used to design a more detailed study.

Based on the conclusions from our review of the draft protocol, we believe that the study objective needs to be more clearly defined for the stakeholders, particularly the studied communities and the regulatory agency representatives that communicate with the public. To achieve this end, we recommend that the study objective be redefined in the protocol and that discussion of the objective should be consistent in both the protocol and during presentations to stakeholders.

The Quality Assurance Project Plan of the Environmental Monitoring Assessment component of the study (Appendix A of the draft protocol) lists several objectives in Section 6 that the air quality monitoring network is designed to achieve. One of the objectives of the ambient concentration measurements that will result from the monitoring network is to estimate potential health risks for the local populations. This objective appears to be beyond the scope of the project as outlined in Part III, Narrative Statement, of the draft protocol. The health study has been designed to meet the concerns of U.S. EPA Region 7 and the local citizens as defined in the Narrative Statement, which is whether environmental releases from hazardous waste combustors and other industries in the study area can be associated with health problems in these communities. The evaluation of potential health risks, i.e., the prediction of the likelihood of adverse health effects based on modeling, was not originally identified as a study objective. In addition, health risk assessments have already been performed for emissions from each of the cement manufacturing facilities, using conservative modeling methodologies.

If the evaluation of health risks for each local population is planned for this study, using results of the monitoring network, then additional information on risk assessment methodology, evaluation and interpretation of monitoring data, and use of the results would be needed in the protocol. On the other hand, if the intended purpose of evaluating potential health risks is solely to locate neighborhood monitoring stations, as has already been performed in the draft protocol, the discussion of the monitoring network objectives should be clarified to reflect this purpose.

### **Relationship Between Chemical Sources and Health Impacts**

As mentioned above, the objective of the Health Study as stated in the draft protocol is to determine whether an association exists between any health problems in the subject communities and environmental releases from hazardous waste combustors and other industries in the study area. The protocol describes study elements that are designed to identify environmental sources of chemical exposures that could be associated with observed health effects in the study communities. The elements of the study that will be used to identify potential sources of exposures are contained in the Environmental Monitoring Assessment section of the draft protocol. The following comments refer to the Environmental Monitoring Assessment component of the study.

#### *Objectives of the Environmental Monitoring Assessment*

The draft protocol states that the Environmental Monitoring Assessment component of the study may be used for two purposes: (1) to determine temporal and spatial distribution of air contaminants in the region in support of the health effects evaluation; and (2) to infer cause-effect relationships of exposures to specific chemicals. We believe that design of the Environmental Monitoring Assessment component of the study is limited in its ability to determine whether cause-effect relationships will or will not be observable from the study results. Limitations in the monitoring study design include the timing of air sampling, the locations of sampling stations, and the lack of personal exposure monitoring.

In the introductory paragraphs of Section 6 of the draft protocol, an additional objective is stated that air monitoring data will be used to estimate potential health risks for the local population. The intent of the health risk assessment is unclear in this section of the protocol. Although risk assessment is used in later sections of the protocol to locate neighborhood monitors, it is not clear how risk assessment will support the original objective of the study to determine whether there are associations between health effects and environmental releases. See Study Objective comments above.

#### *Scale of Monitoring*

The draft protocol points out under *Objectives and Design Criteria* the difficulties in linking ambient air concentrations to actual personal exposures to chemicals. Individuals are exposed to chemicals from multiple sources over the course of a day. As described in the draft protocol, the study will not attempt to determine any individual's actual exposures. Without information on personal exposures, the study will be limited in its ability to identify whether chemicals in ambient air, or which chemicals, can be related to an individual's actual exposure. This limitation will further limit the ability of the study results to associate any chemical exposures, regardless of source, with any health conditions.

## *Monitoring Methodology*

Three types of ambient air monitoring scales are planned for the study. For the *Regional* scale monitoring, the downwind station will be located at or near the point of maximum predicted concentrations of chemicals in air, based on results of air dispersion modeling. The upwind station is identified as located 180 degrees from the impact station. However, winds that shift in direction over the short-term will cause chemicals in ambient air to transport to the "upwind" station. Although the protocol mentions in Section 9.1 that comparisons of measurements from the upwind and downwind sites will be analyzed in conjunction with meteorological data, the protocol does not clearly describe how the samples will be identified as upwind or downwind, and how they will be analyzed with respect to the effect of shifting winds. The lack of a clear distinction between upwind and downwind samples will further limit any ability to identify sources of sample chemicals.

As stated in Section 8 of the draft protocol, an alternative method will be used for monitoring PM<sub>10</sub>. However, the protocol does not provide a detailed description of the methodology that ensures the accuracy of the measurements. Although the protocol indicates in Section 8 that results of the ambient air monitoring will not be used for comparison with national standards, the National Ambient Air Quality Standards (NAAQS) are nonetheless mentioned in Sections 6.2.4 and 8.1.2 as criteria that will be used for comparison of measured ambient air concentrations. If comparisons to NAAQS are planned for the monitoring data, then U.S. EPA-approved methods and equipment should be used for data collection.

Section 6.4 mentions the use of *special purpose* community monitors to be located at community monitoring sites determined by the community residents and local officials. The data are to be collected by members of the local community. The protocol does not describe how the personnel for data collection will be trained and what quality assurance measures will be in place to ensure accuracy of the data.

Each of the study communities has multiple potential sources of volatile organic compounds (VOCs) that could be measured by the ambient air monitors. However, the draft protocol does not address how the multiple sources of VOCs will be evaluated during the identification of potential sources for the chemicals measured in ambient air.

## *Data Evaluation and Conclusions*

The draft protocol provides limited information on how the data from the monitoring network will be evaluated and how the data will be used to reach conclusions consistent with the objectives of the study. Specifically, the protocol should describe how data validation will be performed, how the effects of variable wind directions will be addressed in data retrieval and interpretation, what quality control and quality assurance measures for laboratory analyses will be used, how non-detected values and data outliers will be evaluated, and what level of analytical precision will be used for laboratory analyses. Although an objective of the health study is to identify the sources of chemicals in ambient air that can then be associated with observed health conditions in the local populations, the draft protocol for the ambient monitoring component of the study does not present details of an approach for using the monitoring data to identify the likely sources of the measured chemical concentrations.

The draft protocol indicates in Section 8.3.2 that a single PM<sub>10</sub> sample will be analyzed for metals in each of the communities. Additional PM<sub>10</sub> samples will be analyzed only if concentrations of metals exceed health criteria. A single sample for each community does not appear to be adequately representative of ambient air conditions in a community. We recommend that additional samples in each community be considered for the PM<sub>10</sub> analyses.

### *Integration of Chemical Monitoring Results and Health Study Results*

The draft protocol provides limited information about how the ambient air monitoring program results will be integrated with the results of the health study. Specifically, the protocol (1) does not identify criteria for evaluating the ambient air data, (2) does not describe how the ambient air data will be used to identify sources of chemicals that are measured in the neighborhood monitoring stations, and (3) does not present a detailed approach for using the monitoring data to identify the chemical exposures to the study population. Finally, the draft protocol is unclear as to how the data from the ambient air monitoring program will be used with data from the respiratory study and cancer data to make an association of chemical exposures with health effects.

### **SPECIFIC COMMENTS**

The following provides specific comments on the limitations of the Respiratory Health Study to meet the stated study objectives.

#### *1. Population Sizes*

The draft protocol does not adequately demonstrate that the number of communities and individuals to be studied in both the respiratory study and the cancer incidence study are sufficient to observe differences between the study and control groups.

The Respiratory Health Study component of the study identifies four communities in which hazardous waste combustors are located as the study communities. The control community selected is a single control community that is "upwind" of the study area. The protocol does not demonstrate that a single control community or that a population of 50 individuals from the control community will be adequate for a statistical comparison with 50 individuals from each of the four study communities. Criteria for identifying a control community and how the "upwind" community of Sedan met those criteria should be described in more detail.

The draft protocol describes how the study and control subjects will receive a questionnaire, medical examination, and lung function tests. From each community, 50 individuals with decreased lung function will be identified for the lung function tests, which are performed twice during the study - once as a baseline and once more at the end of one year. The protocol states that this number of individuals and data points (i.e., two data points per individual) are sufficient to generate regression lines comparing symptoms and loss in lung function over the course of one year. However, the protocol does not demonstrate whether this number of individuals and data points will provide sufficient information (statistical power) to observe differences between the study communities and the single control community of 50 individuals.

Another concern of the study protocol is that it does not address "confounders", which are variables outside of the study parameters that can impact the results of the study. For example, the protocol does not discuss how the study will address the potential confounding effects of short-term weather conditions on the single lung function tests performed after one year. For example, it is established that occurrence of respiratory illness tends to increase during inclement weather.

Also, the small number of individuals and the single data point at the end of one year will result in low statistical power of the study. As such, the ability to detect a statistically and biologically significant increase in adverse health effects after one year, compared to control and against typical background variability, will also be low.

The cancer study is designed to collect cancer incidence and prevalence data for the communities and counties of the study and control populations. By using statewide cancer mortality data, the number of deaths from each type of cancer in each town can be predicted based on the population of the town. The predicted mortality will then be compared with the actual cancer mortality data for each town to determine if the rates differ between towns. However, the protocol does not present a discussion on the limitations of using small populations in cancer prevalence and mortality studies. The protocol does not discuss whether the small sizes of the populations will be sufficient to detect differences in cancer prevalence or mortality between a study community and the control community.

## 2. *Selection of control community*

The selection of the control community does not appear to be adequately justified based on the objective of the study that is stated in the draft protocol, i.e., to assess possible adverse health effects from burning hazardous waste. Ideally, with all other variables properly controlled, the only difference between the study and control populations should be the burning of hazardous waste in the study communities. In other words, the burning of hazardous waste would be the only difference between the two populations, and any other sources of airborne chemicals (i.e., non-hazardous waste related) would be controlled.

However, the control community that was selected is not controlled with respect to the other variables that may contribute to airborne chemicals, such as the combustion of non-hazardous waste, industrial combustion of fossil fuels, and other industrial sources of chemicals in the environment. All of these variables can be found in the study communities, but appear to be lacking in the control community. In addition, the protocol does not discuss whether the communities may be exposed to different levels of agricultural chemicals that may contribute to pediatric cancers. If the variables that contribute to airborne chemicals are lacking in the control community, the study will be comparing a study community with multiple sources of fossil fuel combustion emissions with a control community that has limited fossil fuel combustion, rather than communities with and without hazardous waste burning. The draft protocol does not document that the additional variables that affect exposures due to other than hazardous waste burning will be controlled in the study. As a result, these variables have the potential to confound the study results.

3. *Method of selecting respiratory study subjects*

The method of selecting subjects for inclusion in the Respiratory Health Study component of the study has not been carefully described in the draft protocol. The Respiratory Health Study relies on voluntary participation in the health survey and filling out a questionnaire. Such voluntary participation in the health survey and filling in the questionnaire may be biased in favor of those people who have preexisting health problems; resulting in the over-representation of individuals of poor health in the study population. The problem of subject bias in performing community health surveys has been documented in the scientific literature. Reasonable attempts should be made to minimize the potential for subject bias, such as the use of assistants to help fill in questionnaires.

In addition, the draft protocol does not indicate whether the final populations of subjects that have been randomly selected from each community will be evaluated to ensure that the population-related confounders are minimized.

There is also no indication in the draft protocol whether the study will determine the demographic and health characteristics of the study group as well as those who refuse to participate in the study. If this information demonstrates that the population participating in the study differed in potential confounders from the population that refused to participate (e.g., different medical histories, types of exposures to airborne chemicals), then the results of the study would be impacted (confounded).

4. *Adequacy of health measurements*

The draft protocol indicates that the American Thoracic Society (ATS) questionnaire that will be used in the Respiratory Health Study will also be used to investigate the incidence of cancer. While the ATS questionnaire is adequate for examining respiratory health endpoints, the questionnaire contains limited questions on a subject's history of cancer diagnosis. Therefore, it is inadequate for use in cancer epidemiology investigations. Additional questions relating to cancer risk factors and other confounding variables would need to be developed, validated, and used in the questionnaire component of the study in order to investigate cancer as a health endpoint.

The protocol lists pediatric cancers as endpoints of concern in the study. The following are typically considered necessary types of information when studying pediatric cancers: cancer incidence, mortality, age of onset of cancers in first-generation relatives, parental occupations, and other parental behavior and habits that might adversely affect spermatogenesis and gestation. This information will not be gathered with the ATS questionnaire.

There is reference in the study proposal to a previous investigation on pediatric cancers in Kansas. However, cancer development has a long latency period, up to 20-30 years, and most childhood cancers develop too soon to be associated with environmental exposures. Childhood cancers are also known or suspected to be mainly genetic in origin and etiology.

The example questions listed above are designed to provide the needed information on family history and genetics that is not on the ATS questionnaire.

In the cancer component of the study, cancer prevalence and mortality data will be collected from state databases and the National Cancer Institute database. However, it should be noted that cancer data obtained from cancer registries typically do not have information on other variables associated with the etiology of cancer (e.g., smoking, ). These other variables could confound potential associations of cancer incidence with the presence of airborne chemicals. The protocol is unclear on how the study will account for these unaccounted variables in the databases.

As described above, 50 individuals with decreased lung function will undergo the lung function tests. The lung function tests are performed twice during the study - once as a baseline and once more at the end of one year. The protocol states that this number of data points (i.e., two data points per individual) are sufficient to generate regression lines comparing symptoms and loss in lung function over the course of one year. However, the protocol does not demonstrate whether this number of data points will provide sufficient information (statistical power) to observe differences between the study communities and the single control community of 50 individuals.

Lung function tests are less susceptible to sample and subject bias than the questionnaires, and may be more sensitive than the cancer prevalence and mortality data for the size of the study population. However, the use of only two periods of testing, both during the same season of the year, limits their usefulness in the study. The low frequency of testing could be confounded by seasonal effects on lung function. The study would benefit from more frequent performance of the tests to control for potential seasonality and weather effects on lung function.

The draft protocol does not mention whether biomarkers have been considered for measuring chemical exposures to individuals in the study. Since the ambient air monitoring program will not use personal monitors to determine individual exposures to chemicals in the environment, the measurement of biomarkers could be useful in identifying actual chemical exposures.

5. *Adequacy of data collection methods for hospitalizations*

Based on the draft protocol, the information to be gathered regarding hospitalizations could be impacted by confounding factors. The draft protocol does not indicate how confounding factors in hospitalization will be accounted for in the respiratory study.

Confounding factors in hospitalization can include differences in access to hospital care, use rates, fee rates, disease classification procedures, and medical record-keeping of the hospitals. Additional confounders include differences among communities in the percentage of people who have hospital insurance and in the number of hospitals that participate in the study.

Evidence that these confounders can affect the success of epidemiology studies comes from successful studies performed in Canada that have shown that universal medical coverage and standardized data recording and collection methods minimizes hospitalization confounders (Burnett et al. 1997, 1998; Sueb et al. 1996).

6. *Statistical analytical method for multiple communities*

The draft protocol does not indicate whether multi-community statistical analytical methods will be used. The Canadian studies mentioned above and the Harvard "6 and 24 City" study (Ware et al. 1986) also used multiple cities or communities in their investigations. The statistical technique recommended in those studies is a nested logistic regression analysis in which the community or city is considered to be the sampling unit. This method reduces inter-community variation, which is a large source of variability in multi-city studies.

7. *Population stratification based on age*

The draft protocol indicates that population data for the cancer component of the study will be stratified by decade, for example, 0-9, 10-19, 20-29, etc., to calculate and compare mortalities among the study groups. However, over-stratification of the population can reduce the statistical power of the results. This would further impact this study that already has low statistical power for the reasons mentioned above. A more appropriate stratification of the population would be the grouping by "stages of life", e.g., ages 1-10, 11-18, 19-40, 41-65, and over 65.

## **OTHER COMMENTS**

In addition to the above *General* and *Specific* comments, we provide the following comments on the language and terminology that are contained in the draft protocol. The comments primarily focus on the incorrect or inappropriate use of toxicology and risk assessment terms.

Page 10 - The use of the term *toxins* in Section C of the draft protocol is inaccurate. The term *toxins* applies specifically to natural chemicals that are produced by biological organisms as a deterrent or poison, and are found principally in poisonous plants, bacteria, and animals such as snakes and spiders. The term *chemicals in air* would be a more appropriate expression in this section of the protocol.

Page 10 - The identification of chemicals as *toxic agents* is unnecessary as all chemicals can be shown to be toxic under some condition of exposure. The conditions of exposure from the ambient air concentrations may be insufficient to cause toxicity in exposed individuals. In this case, the use of the term *toxic agent* to describe a monitored chemical could be misleading.

Page 32 - The protocol text states that a "*hazard index of greater than unity indicates that adverse health effects will occur from exposure to the pollutant(s), while a hazard index of less than unity indicates that adverse health effects will not occur from exposure to the pollutant(s)*". This definition of a hazard index is both incorrect and very misleading. The U.S. Environmental

Protection Agency specifically states in guidance for performing human health risk assessments (USEPA 1989, 1997) that a hazard index greater than unity indicates the need for further detailed analysis of chemical-specific hazards by organ and exposure route. It does not define a hazard index greater than unity as indicating that adverse health effects will occur.

U.S. EPA further states that an organ-specific and route-specific hazard index (termed a "segregated hazard index") that "...exceeds unity indicates a potential for noncancer health effects. As a rule, the greater the hazard index value is above unity, the greater the concern for noncancer health effects." Again, the exceedance of unity does not indicate adverse health effects, but does indicate concern over the potential for health effects. Because the hazard index method for evaluating noncancer health risks is not probabilistic, the actual likelihood of an adverse effect when a hazard index (or a segregated hazard index) is greater than unity cannot be determined.

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