



HEALTH EFFECTS INSTITUTE

Nitrogen Dioxide and Respiratory Illness in Children

Part III: Quality Assurance in an Epidemiologic Study

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HEI HEALTH EFFECTS INSTITUTE

The Health Effects Institute, established in 1980, is an independent and unbiased source of information on the health effects of motor vehicle emissions. HEI studies all major pollutants, including regulated pollutants (such as carbon monoxide, ozone, nitrogen dioxide, and particulate materials), and unregulated pollutants (such as diesel engine exhaust, methanol, and aldehydes). To date, HEI has supported more than 120 projects at institutions in North America and Europe.

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I. INVESTIGATORS' REPORT William E. Lambert et al. 1

This volume contains Part III of a report on Nitrogen Dioxide and Respiratory Illness in Children. Part I, which describes the health outcomes, and Part II, which presents the exposure data, were published together with a Commentary by HEI's Health Review Committee in June 1993. Part III describes the Quality Assurance and Quality Control procedures used, and provides supporting documentation for the other parts of this Research Report.

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II. RELATED HEI PUBLICATIONS 33

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Nitrogen Dioxide and Respiratory Illness in Children

Part III: Quality Assurance in an Epidemiologic Study

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ABSTRACT

This report describes the quality assurance and quality control program developed for the previously reported epidemiologic study of nitrogen dioxide (NO₂)* and respiratory illness in children (Health Effects Institute Research Report 58, Parts I and II). The specific aims of the program were to make certain that data were sufficiently accurate, complete, verifiable, and retrievable. The quality assurance and quality control program consisted of: a written protocol, standard operating procedures, written records, a project management system, appropriate data processing, data verification, and data analysis planning, and was staffed by qualified and appropriately trained personnel.

Within the activities of the overall program, two focused quality assurance studies were conducted. During the first of these focused studies, parents maintained a calendar-diary of their child's daily respiratory symptoms. Telephone interviews were conducted at intervals of two weeks, and parents used the calendars to report on symptom occurrence since the previous call. To assess the comparability of illness events based on symptom reports from the parents with usual clinical diagnostic methods, nurse practitioners examined children during illnesses, and office and clinic

records of outpatient visits were reviewed. Using the parent reports, respiratory illnesses were defined as symptom episodes of at least two consecutive days; lower respiratory illnesses included at least one day of either wet cough or wheeze. Runny or stuffy nose was reported for 93% of illnesses; and wet cough for 33% and wheeze for 6% of illnesses. In comparison with the diagnoses made by a nurse practitioner, parent reports of wet cough or wheeze were sensitive (93.4%) for detecting lower respiratory illnesses, but nonspecific (with specificity of only 24.2%). The majority of the false-positive lower respiratory illnesses had the symptom of wet cough. The comparison of parent reports with outpatient records provided similar findings. These findings indicate that standardized reporting of respiratory illnesses can be achieved with regular telephone interviews, but the classification of specific illnesses from the observations of parents' information may differ from diagnoses made by clinicians.

The second focused quality assurance study evaluated the measurement error associated with the parents' use of passive diffusion samplers for NO₂. Midway through the study, technicians conducted home visits to assess compliance with stated procedures, and to make independent measurements of NO₂. Based on criteria for placement and use of the samplers, conditions of noncompliance were observed on about 40% of visits. However, the consequences for accuracy were small; the mean difference between two-week average NO₂ concentrations measured with samplers deployed by technicians and those deployed by parents was 0.3 parts per billion (ppb) (SD = 4 ppb). These findings may be partly explained by the use of strict criteria for placing the samplers. Nevertheless, 22% of samplers were opened later than the times reported by parents. These delays were found not to have a substantial impact on the accuracy of measurements, possibly because of the gradual variation in concentrations between sampling periods and the usually short delay (median = 1 day) relative to the 15-day sampling period. These findings suggest that although parents deviated at times from the protocols for sampler placement and opening and closing, the consequent misclassification of exposure was small in most cases.

* A list of abbreviations appears at the end of the Investigators' Report.

This Investigators' Report is Part III of the Health Effects Institute's Research Report Number 58. Parts I and II (Health Outcomes by Samet and colleagues, and Assessment of Exposure to Nitrogen Dioxide by Lambert and colleagues) were published by the Health Effects Institute in June of 1993. Parts IV and V, which address monitoring of ambient NO₂, are forthcoming. Correspondence regarding this Investigators' Report may be addressed to Dr. William E. Lambert, Epidemiology and Cancer Control Program, Cancer Research and Treatment Center, University of New Mexico Medical Center, 900 Camino de Salud NE, Albuquerque, NM 87131-5306.

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Although this document was produced with partial funding by the United States Environmental Protection Agency under assistance agreement 816285 to the Health Effects Institute, it has not been subjected to the Agency's peer and administrative review and therefore may not necessarily reflect the views of the Agency, and no official endorsement should be inferred. The contents of this document also have not been reviewed by private party institutions including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties, and no endorsement by them should be inferred.

The quality assurance and quality control program and the two focused quality assurance studies provided valuable information for the management of the longitudinal study and the interpretation of the study's findings. The quality assurance and quality control program successfully monitored the quality of the data and allowed adjustments in collection methods; and the focused quality assurance studies demonstrated the validity of the methods used to measure respiratory illnesses and NO₂ exposures. Although these activities required considerable time and effort, they enhanced the quality of data needed to test the hypothesis that exposure to NO₂ increases the incidence and duration of respiratory illnesses in infants.

INTRODUCTION

Observational data from epidemiological studies may be limited by lack of validity and reliability, and the literature is replete with methods for controlling and detecting bias and for standardizing data collection procedures. Although data quality has typically been a paramount concern in the design, analysis, and interpretation of epidemiologic studies, few formalized and comprehensive quality assurance and quality control (QA and QC) programs have been described for observational studies.

Epidemiologic research has played a prominent role in the assessment and management of human health risks of environmental pollutants. The potential limitations of observational data have been a source of uncertainty, and have led to widespread recognition of the need for QA and QC activities in studies that have regulatory implications. Guidelines were proposed by the Interagency Regulatory Liaison Group (1981) and by the Chemical Manufacturer's Association (1991). Analogous guidelines have been published for other types of scientific data having similar regulatory import. For example, the U.S. Food and Drug Administration established procedures termed "Good Laboratory Practice" for studies on the safety of food additives and pharmaceuticals (U.S. Food and Drug Administration 1987). Similarly, the U.S. Environmental Protection Agency established good laboratory practices for evaluating pesticides and toxic substances (U.S. Environmental Protection Agency 1983, 1989).

The Health Effects Institute has recognized the need for formal QA and QC programs in all of its investigations. In its Requests for Applications, the Health Effects Institute directs that funded studies use "appropriate good laboratory procedures and quality assurance and quality control procedures" and specifies that "data are [to be] acquired under well-defined conditions that are reliable and traceable". In

1987, as this epidemiologic study of NO₂ and respiratory illness was implemented, a QA and QC program was needed that met the intentions of Health Effects Institute Guidelines, which were oriented towards experimental research.

In this report, we describe the QA and QC program applied to this epidemiologic study. The principal findings with regard to NO₂ and respiratory illness in children have been previously reported in the Health Effects Institute Research Report Number 58, Parts I and II (Lambert et al. 1993; Samet et al. 1993).

SPECIFIC AIMS

The goal of the QA and QC program was to maximize the reliability and validity of data by applying a system of checks designed to feed information back to project management in time for corrective action. The specific aims of the program were to collect data that were sufficiently accurate, complete, verifiable, and retrievable. Within the activities of the overall program, two focused QA studies were conducted to assess the extent of misclassification of respiratory illnesses and NO₂ exposure, the two most crucial aspects of the study protocol. The two special studies used intensive methods of measurement that were not practical to use in the main study.

This report describes in three sections (1) the overall QC program, (2) the QA activities related to measuring respiratory symptoms and illnesses, and (3) the QA activities related to NO₂ exposure measurements.

SECTION 1: THE QUALITY CONTROL PROGRAM

INTRODUCTION

The term "quality control" refers to checks on the quality of the data performed during routine activities. These checks were designed to maximize the consistency (reliability) of the data collected by the different members of the research team throughout the period of data collection. The term "quality assurance" addresses activities that assessed the validity of the data using methods and personnel that were independent from those routinely used.

ELEMENTS OF THE QUALITY CONTROL PROGRAM

The elements of the QC program (Figure 1) were (1) a written protocol, (2) qualified personnel, (3) standard operating procedures, (4) written records, (5) a project management

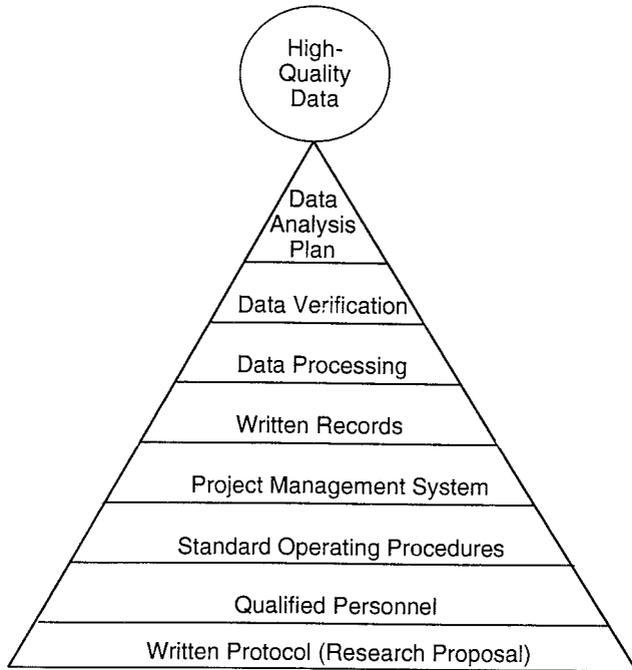


Figure 1. Quality assurance and quality control program components.

system, (6) appropriate processing of data from questionnaires and NO₂ samplers, (7) data verification, and (8) a data analysis plan.

Written Protocol

The original written proposal to the Health Effects Institute served as the principal description of the research questions, study design, and exposure and outcome measures.

Qualified Personnel

The research proposal and job descriptions documented the primary responsibilities for each staff position. To supplement these documents, curriculum vitae were kept on file to document the education and work experience of each person. In addition, a record of training was maintained for each employee (Figure 2).

Standardized methods of training for nonmanagement personnel included a general review of indoor air pollution, orientation to the project, techniques of interviewing and assessing housing characteristics, and principles of operation for the passive diffusion samplers. Role-playing and practice home visits were used to develop skills.

Nurses and nurse practitioners were trained in methods of medical history taking and physical examination by the Project Pediatrician (Dr. Alice Cushing) and the Principal

Employee Name _____
 Position _____
 Start Date ____/____/____

UNM STUDY OF INFANT RESPIRATORY ILLNESS
 PERSONNEL TRAINING RECORD

Protocol	Comments	Date	Initials
Recruitment and Screening Interview			
Home Survey			
NO ₂ Sampler Placement			
NO ₂ Sampler Tracking			
Symptoms and Illness Telephone Call			
Nurse Practitioner Home Visit			
Symptom History and Physical Exam			
Oximetry			
Tympanometry			
Nasal Wash			
Virology Laboratory Protocols			
Nasal Wash Specimen Tracking			

Figure 2. Example of record sheet used to document personnel training.

Investigator. This training was performed using subjects from clinics and the study; the competency of the nurses and nurse practitioners was established by the Project Pediatrician.

Standard Operating Procedures

Standard operating procedures are written statements of the conduct of routine operations, and were prepared by the Principal Investigator and the Project Coordinator. The procedures followed a standard format (Figure 3) and included the purpose, principle, and source of the procedure, the responsible personnel, a step-by-step description of the procedure, and examples of the records and forms. A document control system was used to track revisions to the standard operating procedures and dates of implementation (Figure 4). As an example, Appendix A contains the standard operating procedure developed for home visits made to assess housing characteristics and to place the passive diffusion samplers for NO₂. As necessary, procedures were updated and exchanged for the superseded version.

The standard operating procedures were organized into

- 1.0 INTRODUCTION
 - 1.1 Purpose
 - 1.2 Principle of the Procedure
 - 1.3 Sources of the Procedure (if applicable)
 - 1.4 References (if applicable)
- 2.0 RESPONSIBILITIES
- 3.0 EQUIPMENT
- 4.0 PROCEDURE
 - 4.1 Preparation
 - 4.2 Step-by-step Operation
 - 4.2.1 Sub-Operations
 - 4.3 Calculation or Preparations for Data Entry
 - 4.4 Quality Control and Quality Assurance Checks
 - 4.5 Standards and Blanks (if applicable)
 - 4.6 Calibration (if applicable)
 - 4.7 Maintenance (if applicable)
- 5.0 RECORDS
 - 5.1 Data Collected by this Procedure
 - 5.2 Record Forms
 - 5.3 Location and Placement of Forms
- 6.0 FORMS
 - 6.1 Blank Forms
 - 6.2 Question-by-Question Specifications
- 7.0 APPENDICES
 - Approval
 - Revision Record
 - Distribution Cover Sheet

Figure 3. Outline of standard operating procedures.

a Manual of Operations that was given to all personnel during training. The procedures were supplemented by a general description of the study and the hypotheses to be tested. General topics relevant to the conduct of research, including confidentiality, informed consent, and interviewing techniques also were discussed in the manual.

Written Records

Questionnaires and forms used in the study were designed to be appropriate for all mothers of the research subjects. During October through December 1987, all questionnaires were tested to refine and validate the methods. Multiple-choice options were selected to be exhaustive and mutually exclusive. To minimize respondent burdens, questions dependent on previous answers were noted to be skipped. The forms were precoded to standardize and facilitate data processing. Appendix B contains the Home Characteristics Questionnaire and the Home Visit Medical History, which illustrate how these concepts were implemented.

FORM 2.4
(07/22/88)
Revision 1
Page 1 of 3

Figure 4. Example of header used on data collection instruments for document control.

During the course of this prospective study, decisions and their rationale were documented in contemporaneous memoranda to the staff and to project files. As appropriate, questionnaires, forms, and standard operating procedures were revised and older versions were archived.

Project Management

During design and implementation, the Principal Investigator and the Project Coordinator identified key events and information critical to monitoring the progress of the study. A computerized tracking system using FoxBASE+ software (Fox Software, Inc., Perrysburg, OH) was developed to monitor subject enrollment and attrition, the measurement of respiratory symptoms and NO₂ exposure, and data entry. This information was synthesized into tracking reports for the Principal Investigator and Project Coordinator (Figure 5).

Regular staff meetings, in-service training sessions, and telephone conference calls were held to review progress, and to discover and solve problems. Proposed revisions to the study design or standard operating procedures were reviewed and approved by the Principal and Coinvestigators.

The organizational chart for the project is presented in Figure 6. The Principal Investigator was ultimately responsible for the completeness and quality of the data collected. The Project Coordinator was responsible for the day-to-day management of data collection. With the Principal Investigator, the Coinvestigators implemented the study and supervised activities related to specialty areas including pediatric clinical assessments, virology, NO₂ exposure, and statistical analysis.

Data Processing

Two data processing systems were established to accommodate data handled by the University of New Mexico (UNM) and the Harvard School of Public Health (Figure 7). The University of New Mexico was responsible for the processing of all data collected by interviews and on data sheets; Harvard was responsible for laboratory analysis of the NO₂ samplers and QC of exposure measurements.

UNM Study of Infant Respiratory Illnesses
 Progress Report
 Up to 04/04/90

Number of active homes with gas stoves	483
Number of active homes with electric stoves	156
Number of active outdoor sites	11
Status	
Active participants	639
Participants on vacation	4
Participants who completed protocol	228
Participants who dropped out	333
Reason for dropping out or release from study	
Mother began smoking	7
Other household member(s) began smoking	17
Moved out of town	82
Subject in full-time day care	88
Declined to participate further	50
Noncompliant	48
Moved without notice, lost	24
Other	17
Total person-months of monitoring completed	15,987

Figure 5. Sample report of cohort follow-up status from the computerized tracking system.

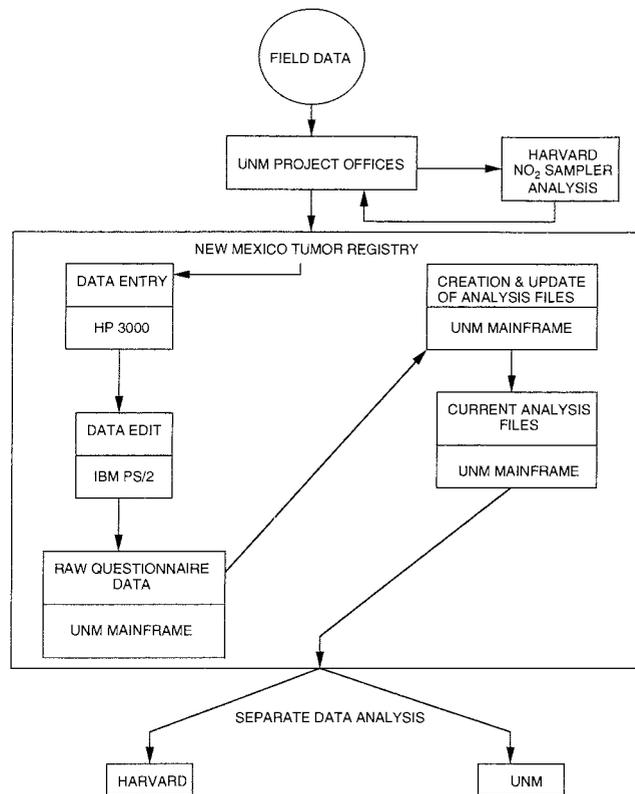


Figure 7. Overview of project data management.

Handling and Entering Questionnaire Data into the Computer. A flow chart describing the entry and processing of questionnaire and data sheets at UNM is presented in Figure 8. Before submission for keyboard entry, original data sheets were proofread and corrections to queries were initialed and dated. Data sheets then were assembled into batches and logged into a computer-based tracking system. Duplicate listings of the forms and subject identification numbers within each batch were printed and filed in the

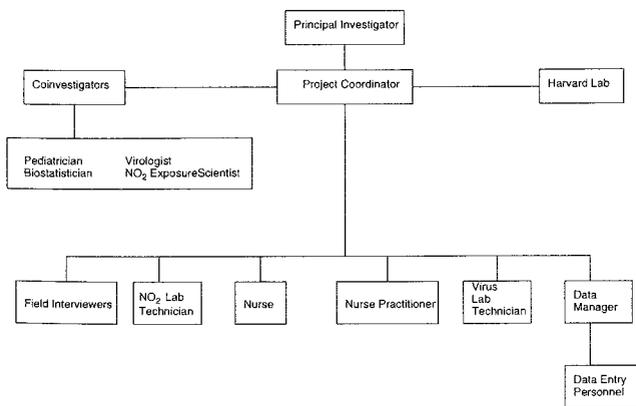


Figure 6. Project organizational chart.

project offices and at the data entry station. Keyboard entry of the data was performed using VIEW data entry software (VPLUS/V Software, Hewlett Packard, Cupertino, CA). For each entry field, the allowed range of values was restricted (e.g., month values 01 to 12).

After entry, the data files were converted into SAS data sets (Statistical Analysis Software, Cary, NC) and programs were run to verify the consistency of responses within each questionnaire (e.g., the presence of a gas cooking stove when pilot lights were indicated). Inconsistencies were counted by the type of questionnaire and question number. For certain "critical" data items (e.g., NO₂ sources), all detected inconsistencies were resolved by correction against original data sheets. For "noncritical" items (e.g., count of number of pets in the home), failure rates were computed but corrections were not made unless consistent or extensive problems were identified. Using these reports, the Data Manager and Project Coordinator monitored the accuracy of data entry throughout the study. After correction of the entered data, the files were appended to larger files.

At intervals, longitudinal checks of consistency were made on repeated questionnaire interviews and checks were made across types of questionnaires. For example,

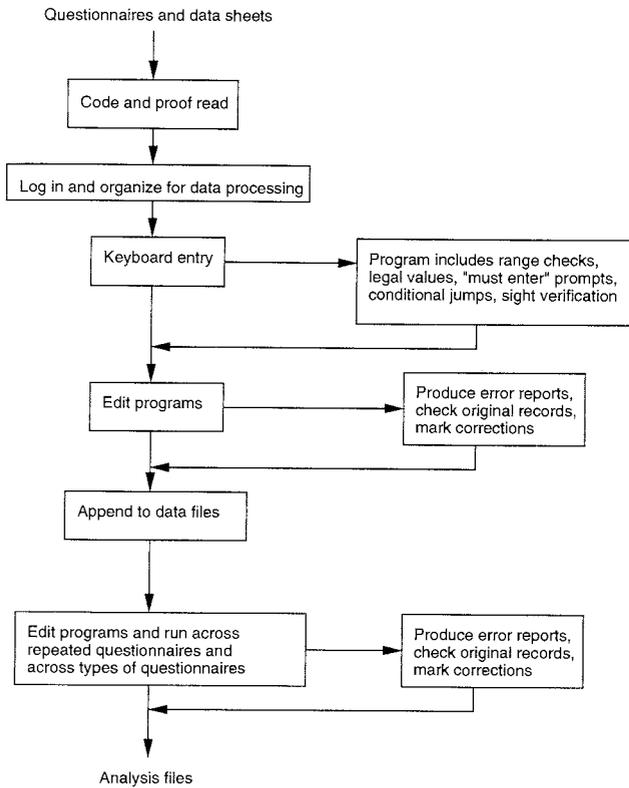


Figure 8. Data processing flowchart.

temporal profiles of breast feeding status were examined, and unexplained gaps, duplications, and illogical sequences in the follow-up records were identified and resolved. Corrections to the data base were documented by written corrections on the original data sheets, and, if necessary, memoranda were written. The original records were filed by subject identification number and stored in locked, fire-resistant cabinets. Throughout the study, computer files were backed up to tape on daily and weekly schedules.

Several programs were developed using dBASE IV (Ashton-Tate, Irvine, CA) to catalog the data and analysis files. The catalog included the name of each file, creation date (or date of last update), creator, source files, and variable names. Data file contents, variable name dictionaries, and file management and statistical programs were archived on magnetic and paper media. The dBASE program allowed searches by keywords and type of analysis.

Handling and Analyzing Nitrogen Dioxide Samplers. Extensive QC procedures were developed and implemented for handling and analyzing the NO₂ samplers. The samplers were assembled at Harvard and mailed to UNM in sealed bags. When received at UNM, the samplers were logged in and used in sequence by the date of assembly.

Production of tubes was timed to minimize the time of storage before use to no more than 30 days.

Barcode labels and optical scanners were used to facilitate handling the large numbers of NO₂ samplers used in the study. The barcode labels were used in pairs; one label was affixed to the sampler and the other was placed on a data sheet used to record the subject who used the sampler, the room placement, and the times of opening and closing. As the samplers were returned from the subjects, their labels were scanned and data relevant to each sampler was entered into a computer data base. The accuracy of keyboard entry was maximized through the use of a data entry program developed using dBASE IV software with range limits and verification against original written records. Following conventional procedures for documenting custody of samples, shipping lists were generated at UNM. Every one to two weeks, the samplers, shipping lists, and magnetic files of relevant deployment data were sent to Harvard.

When received at Harvard, samplers were verified against shipping lists and UNM was notified of discrepancies. Spectrophotometric analysis of the samplers followed published protocols (Palmes et al. 1976; American Society for Testing and Materials 1988). As part of the QC program for the laboratory, standard NO₂ curves were generated before each analysis run. During sample analysis, reagent blanks were analyzed at intervals to check for zero drift. Absorbance data from the spectrophotometer (Perkin Elmer Corporation, Norwalk, CT) were directly transferred through an interface to a desktop computer and merged with the deployment data furnished by UNM.

Quality control evaluations were performed after the laboratory analyzed each shipment of samplers. Using dBASE programs, the data were screened to identify samplers with measurements below the limit of detection, with missing data, and with tube age in excess of 100 days (date of analysis minus the date of assembly). Additional tests included screening the opening and closing times, evaluating the differences between duplicate measurements, and detecting excessive deviation in NO₂ levels between rooms. This information was assembled into a QC report and magnetic file, and forwarded to UNM. These reports were used to correct the data base and to identify households requiring extra guidance or reinstruction in the use of the NO₂ samplers.

Data Verification

As previously explained, data verification required checks at several levels. Each subject was assigned a unique 5-digit identification number at the time of enrollment. These were generated using a "mod-11" algorithm to vary the last digit so that adjacent numbers differed by more than 1 (e.g.,

09652, 09660, 09679) to minimize errors of transposition and miskeying. All data entry programs contained checks to prevent entry of invalid numbers. Sheets of barcode labels were printed for the identification numbers, and were used throughout the study to identify data sheets and questionnaires for each subject.

Questionnaires and forms were reviewed for consistency and completeness before being submitted to data entry. At the time of keyboard entry, range checks were used to restrict opportunities for error, and logical crosschecks were made to ensure consistency within the questionnaire or form. After appending the newly input data to data files, longitudinal crosschecks were conducted to identify inconsistencies, outliers, missing data, and duplicates. For example, NO₂ measurements in a home's series that exceeded the home's seasonal mean levels by three times the interquartile range were flagged. If the outlying value exceeded certain variances based on stove type and time of year, it was excluded (see Lambert et al. 1993).

In the correction of errors on written records, purported errors were lined out but not obliterated, and corrections initialed and dated. Corrections to computer files were documented to hardcopy records and archived.

Plan for Data Analysis

Before constructing analysis files or testing hypotheses, the overall plan for data analysis was written by the Principal and Coinvestigators. This document identified the rationale for the analyses and the supporting literature. Working papers were prepared for the major components of analysis: health outcomes, exposure assessment, and statistical methods for the analysis of longitudinal data.

EXTERNAL QUALITY ASSURANCE ACTIVITIES

The Health Effects Institute contracted an independent organization, Arthur D. Little, Inc. (Cambridge, MA), to perform QA audits on the research program. Audits were performed by the quality assurance officer, Denise Hayes, M.S., and other scientists with relevant expertise (Gerald Ott, Ph.D., epidemiologist; Frank Cadigan, M.D., pediatrician; and Kenneth Menzies, B.S., and Robert O'Neil, B.S., chemists). Audits were performed quarterly during the first year of data collection, semiannually in the second year, and annually thereafter.

The audits began with an interview with the investigators, and the goals of the particular site visit were agreed upon. In addition to a comprehensive examination of data collection activities, areas of particular concern (e.g., data processing and keyboard entry, and handling and analyzing NO₂ samplers) received more intensive scrutiny. Typically,

a random sample of records of original data were reviewed and tracked through data processing to the computer analysis files.

Standard operating procedures, questionnaires, and data sheets were exhaustively reviewed. The QA team accompanied project personnel on home visits to observe the methods used to measure NO₂ and to examine ill children. The team also observed office and laboratory activities related to telephone interviews, the analysis of passive diffusion samplers for NO₂, and the continuous monitoring of data.

At the conclusion of each site visit, the QA team met with the Principal Investigator and the Project Coordinator to discuss the preliminary findings of their audit. Subsequently, the QA team prepared a written statement of findings that was submitted to the Health Effects Institute. After being reviewed by the Executive Director, the Director of Research, and the Health Research Committee, a copy of the report was forwarded to the Principal Investigator.

SECTION 2: COMPARABILITY OF PARENT REPORTS OF RESPIRATORY ILLNESSES IN INFANTS WITH CLINICAL DIAGNOSES

INTRODUCTION

Diagnosis of specific respiratory illnesses during the first years of life is difficult because children cannot describe their symptoms, and researchers must rely on parent reports and clinical findings. The range of symptoms and signs in parent reports is limited primarily to nasal discharge, cough, audible wheezing, visible respiratory distress, difficulty in feeding, and fever. The usual clinical evaluation includes examination of the pharynx, auscultation of the chest, visual inspection of the tympanic membranes, and, perhaps, tympanometry. In more severe illnesses, clinical evaluation may include chest radiograph, oximetry or arterial blood gas sampling, and the culture of the nasopharynx for respiratory viruses.

In spite of the difficulties of diagnosing respiratory illnesses in infants and young children, their occurrence has been monitored in population-based samples, and examined as an outcome measure in studies of the health effects of both indoor and outdoor air pollution and of the effects of infections on lung growth and subsequent respiratory morbidity (Shy et al. 1978; Samet et al. 1983, 1988; Graham 1990). In many of these investigations, respiratory illness experience was ascertained retrospectively by questionnaire, a technique known to have limited validity (Samet et al. 1983; Graham 1990), or by reviews of visits to health care

providers or hospitalizations, an approach that may detect only the more severe episodes and is influenced by patterns of health care access and utilization. Prospective monitoring for respiratory illness using parent reports of symptoms and signs also has been used in epidemiologic research (Dingle et al. 1964; Monto 1971).

We used this latter type of symptom-based monitoring for respiratory illness in our cohort study. To assess the comparability of illness syndromes based on parent reports with typical clinical diagnoses, a nurse practitioner examined sick children according to a standardized protocol. We also reviewed office and clinic records of outpatient visits for respiratory illnesses for a sample of children.

MATERIALS AND METHODS

Overview

Full details concerning the selection of subjects and the ascertainment of illnesses have been described in a previous report in this series (Samet et al. 1993). That report also provides subject characteristics in detail. Our original data analysis presented in that report is based on observations through June 30, 1991.

Nurse Assessment

During the study, a pediatric nurse practitioner, two family nurse practitioners, one of whom specialized in respiratory diseases, and two registered nurses conducted evaluations of children in their homes. These staff members were trained by the Project Pediatrician and began to collect data only after achieving satisfactory competency with patients evaluated in outpatient settings. The nurses and nurse practitioners made home visits and evaluated symptomatic and asymptomatic children selected at the time of the telephone calls, which were performed at intervals of two weeks. All children with an illness involving wheezing or wet cough at the time of contact and some additional children with other symptoms or no symptoms were selected for evaluation. For symptomatic children, the nurses attempted to time home visits within three to four days of the onset of symptoms. By the nature of the protocol, the nurses were aware that they were visiting a symptomatic or well child, and for a symptomatic child, they knew if lower respiratory symptoms had been reported. The home visits averaged 40 minutes.

The practitioner's evaluations covered respiratory symptoms reported on the calendar-diary, and additional symptoms including sneezing, hoarseness, and trouble sleeping. The physical examination included a general assessment with vital signs, evaluation of the ears with an otoscope, and systematic auscultation of the chest for the presence of

rales, rhonchi, and wheeze. Tympanometry (Microtomp, Model No. 71130, Welch-Allyn, Skaneateles, NY) and pulse oximetry (Nellcor Pulse Oximeter, Model N200, Hayward, CA) were performed. The nurse practitioners and nurses also obtained materials for viral culture by performing a nasal washing with phosphate-buffered saline and a throat swab. The washings were immediately introduced into viral transport medium and placed on ice for transport to the laboratory.

Using the patient history and physical examination, the nurse clinician made a diagnosis, classifying the child as well, ill without respiratory manifestations, or as having a respiratory illness. Upper respiratory illnesses included serous otitis, otitis media, and nonspecific upper respiratory illnesses. The lower respiratory illnesses included croup, bronchiolitis, pneumonitis, tracheobronchitis, and nonspecific lower respiratory illnesses. Criteria for making specific lower respiratory diagnoses were taken from the study of children in Chapel Hill, NC (Denny and Clyde 1986). For QC, the project pediatrician performed a parallel assessment of children on 17 home visits. No significant discrepancies between the pediatrician and the nurse practitioners were noted.

Virology

Nasal wash samples were transported to the Clinical Virology Laboratory at the University of New Mexico School of Medicine and processed within one hour of receipt. Samples from children designated as ill were tested for respiratory syncytial virus with a direct antigen detection system (Pathfinder, Kallestad Diagnostics, Austin, TX). All nasal wash samples were inoculated into standard cell culture lines for the detection of respiratory viruses (Schmidt and Emmons 1989). Inoculated cell lines were monitored daily for cytopathic effect. In addition, at three time intervals after inoculation, the primary Rhesus monkey kidney culture for each sample was tested for hemadsorption using guinea pig erythrocytes (McLaren 1986). When viral cytopathic effect was observed or hemadsorption was detected, the virus responsible was identified using indirect immunofluorescence with virus-specific monoclonal antibodies (Gardner 1986).

Outpatient Record Review

Outpatient records were available for review for a majority of subjects. Outpatient records for respiratory diagnoses were abstracted at the offices of three pediatric group practices, pediatric and family practice clinics of the University of New Mexico Medical Center, and the pediatric clinics of a large group practice and of a health maintenance organization. Records for children who had these

facilities listed as their principal source of health care were reviewed by one nurse according to a standardized protocol.

Calculation of Illness Rates

The calculation of illness rates has been previously described (Samet et al. 1993).

RESULTS

By June 30, 1991, 10,771 illness events had occurred. Illness events were defined as the occurrence of at least two consecutive days of any of the following: runny or stuffy nose, wet cough, dry cough, wheezing, or trouble with breathing. Wheezing refers to a high-pitched musical sound audible during breathing; trouble with breathing was the parents' perception of rapid or labored breathing. The illness events ended with two consecutive symptom-free days. Illness duration was calculated as the number of days from onset of symptoms to the last day with symptoms before the occurrence of two consecutive symptom-free days. Runny or stuffy nose was reported as a symptom in most (93 percent) illness events; in fact, the most frequent symptom pattern was runny or stuffy nose alone (51 percent). With regard to the symptoms of lower respiratory tract

involvement, wet cough (33 percent) was much more common than wheeze (6 percent). A report of breathing trouble was infrequent (5 percent).

Incidence rates per 100 days at risk were calculated for the various types of respiratory illnesses (Table 1). Days at risk were those days of observation during which an illness was not in progress. Because subjects were at risk of illness following two symptom-free days, accrual of days at risk of illness began on the third day after enrollment. After an illness or after any period of seven days or more spent outside the home without health surveillance, counting of days at risk similarly began after two symptom-free days. These mandatory two-day intervals were not included in calculating the days at risk. Only slight variation by gender and ethnicity was apparent. The rates tended to increase with the level of maternal education; consistent trends with household income were not present. Higher rates of illness were observed during the winter season and for children with older brothers and sisters.

The duration of the respiratory illnesses varied by illness type. The median duration for upper respiratory illnesses was six days. For wet cough illnesses, the median was 11 days, and for wheezing illnesses, the median was 12 days.

Through June 30, 1991, 238 evaluations of well children

Table 1. Incidence Rates of Respiratory Illness per 100 Days at Risk by Type of Illness

Determinant	All Upper	All Lower	Lower, Wet Cough	Lower, Wheezing
Gender				
Male	1.57	0.82	0.67	0.14
Female	1.69	0.72	0.60	0.10
Ethnicity				
Hispanic	1.56	0.71	0.58	0.12
Non-Hispanic	1.70	0.82	0.69	0.12
Birth order				
First born	1.34	0.66	0.54	0.11
Not first born	1.80	0.83	0.69	0.13
Maternal education				
≤ 12 years	1.50	0.74	0.59	0.14
13–15 years	1.60	0.76	0.64	0.11
≥ 16 years	1.80	0.81	0.69	0.12
Household income				
< \$10,000	1.52	0.90	0.65	0.23
\$10,000–\$40,000	1.62	0.77	0.64	0.12
> \$40,000	1.67	0.75	0.65	0.09
Season				
Fall/winter	1.96	1.08	0.90	0.17
Spring/summer	1.33	0.48	0.40	0.08

Table 2. Selected Findings from Nurse Assessments of Ill Children by Illness Type from the Calendar-Diary Parent Reporting System

Symptoms Recorded by Nurse	Percentage of Illness Type		
	All Upper (<i>n</i> = 106)	Lower, Wet Cough (<i>n</i> = 413)	Lower, Wheezing (<i>n</i> = 127)
From Symptom History			
Runny or stuffy nose	98.1	98.8	94.5
Dry cough	4.5	24.7	29.9
Wet cough	27.4	95.2	91.3
Wheezing	4.7	11.1	67.7
Difficulty breathing	11.3	16.0	38.6
From Physical Examination			
Nasal discharge or congestion	80.2	84.7	80.3
Wet cough	20.8	61.3	70.1
Rales	0	4.8	8.7
Ronchi	9.4	16.9	33.9
Wheezing	11.3	21.5	45.7

and 679 evaluations of ill children had been made by the project staff. The median interval between the onset of symptoms and the home visit was seven days. Of the 238 evaluations scheduled for children presumed to be well, 55 illnesses were subsequently documented by the parent reporting system. For the remaining 183 visits without an illness in progress, the nurse obtained a history of runny or stuffy nose in 18.6 percent, dry cough in 4.4 percent, wet cough in 5.5 percent, and wheezing in 0 percent. On auscultation of the chest, wheezes and rales were not heard in any subjects and rhonchi were present in seven.

From the evaluations of ill children, the historical information on symptoms obtained by the nurse confirmed the parent reporting system (Table 2). By the nurses' direct observations, wet cough was more frequent in illness episodes

classified as lower respiratory tract. Similarly, the prevalence of abnormal findings on auscultation of the chest (rales, rhonchi, and wheeze) was greater in lower respiratory tract illnesses. Wheezing was more than twice as commonly heard in the chests of children classified by parent reports as having a lower respiratory illness with wheeze versus illnesses with wet cough.

The classification of the illness events based on parent reports was sensitive but nonspecific for the diagnosis of a lower respiratory illness by the evaluating clinician (Table 3). (Sensitivity refers to the proportion of clinician-diagnosed lower respiratory illnesses similarly classified by the parent reporting system.) All but 19 of the 287 subjects diagnosed with a lower respiratory illness were similarly categorized by the parent reporting system; thus, the overall

Table 3. Comparison of Nurse Practitioner Diagnosis with Number of Each Illness Type from the Parent Reporting System^a

Nurse Practitioner Diagnosis	All Upper	Lower, Wet Cough	Lower, Wheezing
Not Respiratory Illness	16	13	2
Upper Respiratory Illness			
Otitis	22	71	8
Unspecified	49	154	24
Lower Respiratory Illness			
Croup	2	3	4
Bronchiolitis	1	9	22
Tracheobronchitis	5	56	32
Pneumonia	0	4	0
Unspecified	11	103	35

^a Each value is the number of illnesses in each diagnostic category.

Table 5. Comparison of Diagnosis at Clinic Visits with Parent Reporting System Classification

Clinic Diagnosis	Percentage of Illness Type	
	All Upper	All Lower
Well (<i>n</i> = 73)	41.1	58.9
Upper respiratory (<i>n</i> = 446)	43.5	56.5
Otitis (<i>n</i> = 372)	48.4	51.6
Upper respiratory, otitis (<i>n</i> = 104)	41.4	58.6
Lower respiratory (<i>n</i> = 122)	4.9	95.1
Asthma (<i>n</i> = 23)	0	100.0

ing have contributed significantly to characterizing the epidemiologic features of respiratory infections (Graham 1990). The surveillance system described in this paper evolved from methods used in the study of Cleveland families during the 1940s and 1950s (Dingle et al. 1964) and in the study of Tecumseh families during the 1960s and 1970s (Monto et al. 1971). Although the feasibility of identifying illnesses by contact with families has been well established, the validity of this approach has not been formally characterized; biases potentially affecting symptom reporting have not been explored and the relationships of syndromes defined by reported symptoms to conventional clinical diagnoses have not been well described.

This study provides further demonstration of the feasibility of using parent reporting approaches. Mothers demonstrated a high degree of compliance in reporting illnesses on the two-week telephone calls. Their symptom reports were generally confirmed in the assessment performed by the project nurses (Table 2). It is possible, however, that concordance between the nurses' and the parents' information was improved by the nurses' awareness of the subjects' symptom status. The illness rates and patterns also were comparable to those documented in earlier studies using similar techniques. In the Tecumseh study, children under one year of age had an average of 6.1 respiratory illnesses annually, of which approximately two were classified as lower respiratory based on productive cough, pain on respiration, or "wheezy breathing" (Monto and Ullman 1974). In the Houston Family Study, home visits were made every two weeks; the overall number of illnesses during the first year of life was approximately nine, of which an average of one was classified as lower respiratory tract illness (Gardner et al. 1984). The rates in our study were higher for children

with siblings and the rates of lower respiratory illnesses were greater for males, which is consistent with findings in other studies (Monto and Ullman 1974; Monto and Ross 1977; Denny and Clyde 1986; Graham 1990).

In this study, most illnesses were accompanied by runny or stuffy nose; the symptoms considered indicative of lower respiratory tract involvement, wet cough and wheeze, occurred in slightly more than one-third of the illnesses. Our goal in classifying illnesses as in the upper or lower respiratory tract was to mirror usual clinical diagnostic practices. Moreover, the toxicologically demonstrated effects of NO₂ on respiratory defenses make lower respiratory tract illnesses the more relevant outcome measure in a study of NO₂ (Samet and Utell 1990).

Comparing the classification of illnesses as upper or lower respiratory tract with both the diagnoses made by the projects' clinicians and by the subjects' physicians indicates that our parent reporting system was highly sensitive to identifying clinically diagnosed lower respiratory illnesses, but also very nonspecific (Tables 3 and 5). Few illnesses diagnosed by a clinician as either a specific lower respiratory tract illness or as a nonspecific lower respiratory tract illness were classified as upper respiratory by our parent reporting system; thus, most clinically diagnosed lower respiratory illnesses are accompanied by a parent's report either wet cough or wheeze. Most illnesses with cultures positive for lower respiratory viruses were similarly classified as lower respiratory illnesses by our parent reporting system (Table 4).

The parent reporting system's lack of specificity for clinically diagnosed lower respiratory illness primarily reflects the classification of illness events with wet cough as lower respiratory illnesses (Tables 3 and 5). In infants and young children, it is impossible to differentiate cough productive of secretions originating in the lower respiratory tract from nasal discharge that has drained into the oropharynx. Specificity is improved by considering only wheezing illnesses as involving the lower respiratory tract, but sensitivity declines.

Assessing sensitivity and specificity against clinical diagnoses as a "gold standard" is limited by the lack of objective and uniform criteria for establishing specific clinical diagnoses and by variability among physicians in their diagnostic practices. In fact, there is no uniformly accepted "gold standard" for clinical diagnoses of respiratory tract illnesses in this age range. Neither clinical history nor physical examination are sufficient. For example, in the Tucson Children's Respiratory Study, no specific sign or symptom in the clinical examination was uniquely linked to the four major lower respiratory illnesses (Wright et al. 1989). In the Tucson study, 94 percent of children with bronchiolitis had

wheezing on exam, but 40 percent of children with pneumonia and bronchitis also had wheezing. Moreover, clinicians most often examine children at a single point in time during an illness. Thus, while the presence of rales or wheezing on auscultation of the chest is highly predictive of lower respiratory illness, the absence of these signs at the time of examination cannot rule out lower respiratory tract involvement. Respiratory illnesses have an evolving constellation of signs and symptoms; the diagnosis made by a clinician may thus depend on the point when it is made. Our parent reporting system, by covering the entire symptomatic period, may lead to a classification discordant with the clinical diagnosis made at a particular time.

Viral cultures are not routinely obtained by clinicians, so the isolation of a respiratory virus cannot be used as an additional "gold standard" for diagnosing the illness events evaluated by the children's physicians. In fact, as in the present study, other community-based surveillance systems have had viral isolation rates of about 30 percent (Monto et al. 1971). The isolation rate in the present study also may have been reduced by obtaining the culture at the mid-point of the illness. The symptoms associated with the viral isolates in this study were compatible with the clinical associations of respiratory syncytial virus with bronchiolitis, and of the parainfluenza viruses with croup and tracheobronchitis (Table 4) (Wright et al. 1989; Graham 1990).

We conclude that specificity for clinically diagnosed lower respiratory illnesses can be gained by separating illnesses with wheezing from those with wet cough and no wheeze. For testing hypotheses directed at the effects of environmental pollutants on lower respiratory tract infections, misclassification may be reduced by separating lower respiratory illnesses with wheezing from those without. This stratification of lower respiratory illnesses was used in analyzing the effects of NO₂ in this cohort.

SECTION 3: SUBJECT COMPLIANCE WITH NITROGEN DIOXIDE MONITORING PROTOCOLS

INTRODUCTION

Passive monitors (or samplers) have been developed for many air pollutants (McCarthy et al. 1991) and are being used more frequently. For example, the general public may readily purchase charcoal canister samplers for home radon monitoring and other passive monitors are sold for carbon monoxide, ozone, microwave oven radiation, and ultraviolet radiation (DSK 1992). In exposure assessments and

epidemiologic studies, passive monitors have been used to measure indoor exposures to nitrogen dioxide (Ryan et al. 1988), carbon monoxide (Lee et al. 1992), and radon (Bierma et al. 1989). In the occupational setting, passive monitors have been used to sample exposure to radiation and several chemical air pollutants (SKC 1993).

A principal advantage of passive monitors is the simplicity of using them. However, proper placement (e.g., away from the direct influence of sources or shielded from the wind) and accurate measurement of the exposure duration are critical to the accuracy of these devices. When deployed by trained personnel, opportunities for misuse are minimized. To reduce costs, passive monitors may be used in a research study by the subjects themselves after instructions have been provided. In a number of recent studies, including this investigation, subject deployment was the principal modality for collecting information on indoor concentrations.

Although researchers utilizing this approach for data collection have recognized the potential threat to data quality posed by failure of subjects to follow protocols strictly, little information is available on subject compliance (Southern California Gas Company 1986). While the measurement precision of passive monitors has been assessed in laboratory and field settings (Palmer et al. 1976; Boleij et al. 1986), the magnitude of error introduced by the subjects could exceed that associated with the physical and chemical principles on which the monitors are based. For most passive monitors, the potential bias from misuse has not been assessed.

In this section of the report, we evaluate the compliance with protocols of our subjects' parents in using one type of passive diffusion sampler for NO₂, the Palmes tube (Palmer et al. 1976). The specific aims of the QC and QA activities reported here were to (1) characterize noncompliance in the use of the samplers and (2) quantify the resulting error in exposure estimates.

MATERIALS AND METHODS

Overview of Study Design

Nitrogen dioxide exposure of each infant in the cohort was monitored from birth to 18 months of age (Samet et al. 1992). At enrollment, technicians conducted home visits to place the samplers in the home and to instruct the mothers on the use of the samplers. Thereafter, the mothers exchanged the samplers on a two-week cycle. Midway through the study, technicians conducted a series of home visits to audit the mothers' use of the samplers and to obtain an independent set of NO₂ measurements using samplers placed by the technicians.

Monitoring Protocols

Subjects were enrolled soon after birth (Samet et al. 1992). At the time of enrollment, home visits were conducted to assess housing characteristics and to train the mothers of the subjects on the use of the passive diffusion samplers. With the mother's help, one sampler was placed in the infant's bedroom. In homes with gas cooking stoves, two samplers also were placed in the living room and kitchen. To minimize error and to obtain a measurement representative of each room, the samplers were placed away from potential sources of NO₂ such as gas cooking ranges and furnaces, and as far as practical from windows and exterior doorways. Criteria for the placement of the tubes are presented in Table 6. The mothers agreed to keep the samplers in these locations throughout the 18 months of their participation in the study. They were instructed to notify the interviewers of a change in placement to ensure that the placement of samplers continued to meet the criteria and that all changes were documented.

Mothers exchanged the samplers every two weeks as part of scheduled telephone interviews. New sets of samplers were mailed to the parents once each month and the exposed samplers were returned to the laboratory using the same packaging. In addition to receiving instructions on sampler exchange during telephone calls, written instructions accompanied each set of samplers. Each of the sampler tubes was labeled with a barcode identification number and the room in which it was to be placed. The tubes were to be exchanged immediately after the telephone call. If the mother could not or did not make the exchange at that

time, she was to record the time and date of the exchange and inform the interviewer on the next telephone call.

The schedule of monitoring varied by type of home and season (Samet et al. 1992). In homes with gas stoves, consecutive two-week measurements were made throughout the year in the infants' bedrooms; in alternating months during the winter, two-week measurements were made in the living rooms and kitchens. In homes with electric stoves, measurements were made in the subjects' bedrooms during alternate two-week cycles throughout the year. For purposes of QC, 5% of the total number of sampler tubes were used as replicates; mothers were instructed to place the replicate samplers side-by-side with the usual sampler tube. In addition, 5% of the sampler tubes were sent to the mothers as "field banks"; these samplers were not to be opened, and thus measured contamination associated with transport and handling.

Quality Assurance Audits

Technicians visited homes to document the parents' use of the passive sampler tubes and to deploy a separate set of samplers. During August and September 1990, 192 homes with gas stoves and 26 homes with electric stoves were randomly selected for QA audits from the total of 400 homes being studied at that time. We limited selection to those families who would still be enrolled in the study during the following winter; no household refused the additional monitoring. The households audited in August and September had participated for three to twelve months in the study. In February and March, 1991, 153 gas-stove homes and 24 electric-stove homes of the original group were audited a second time. Thirty-nine households were not monitored in the second QA survey because they no longer met eligibility criteria and had been released from the study (e.g., the child began to attend day care), or because arrangements for a home visit could not be made.

Audit visits occurred within two days after a regularly scheduled telephone interview. Mothers were not informed that the technicians would be assessing their use of the sampler tubes; rather, the mothers were told that "a technician would be visiting their home to make extra air pollution measurements." During the home visits, the mothers' tubes were left in place and not altered by the technician; a checklist was used to document aspects of her use of the tubes (e.g., moved from original placement, placed in a dead-air space or near a potential source of nitrogen dioxide). The technicians placed a separate set of tubes in the homes according to standard operating procedures and placement criteria (Table 6). Two weeks later, after the next telephone interview, the technicians returned to the homes to perform another audit and to retrieve the comparison set

Table 6. Criteria for Placement of Passive Nitrogen Dioxide Samplers

Potential Interference	Placement Criteria
Floor	1 to 2 m above floor
Sources of NO ₂	2+ m from gas cooking stove 2+ m from gas furnace or spaceheater
Potential sinks	Avoid placement on masonry or houseplants 1 m from windows and exterior doorways
Strong air currents	Avoid placement near heating/cooling vents 2+ m from evaporative cooler vent
High humidity sources	2+ m from humidifiers 1+ m from sink in kitchen

of tubes. Thus, the comparison measurements made by the field technicians lagged by one to two days behind those made by the mothers, but overlapped for the majority of the sampling period. If necessary on the return visit, the use of the sampler tubes was corrected with the parents.

Nitrogen Dioxide Samplers

Indoor NO_2 concentrations were measured using a sampler developed by Palmes and associates (1976). The sampler is constructed of a Plexiglas tube approximately 6 cm in length and 1 cm in internal diameter. When uncapped, air diffuses the length of the tube and any NO_2 present is adsorbed onto stainless-steel screens coated with triethanolamine. The amount of absorbed NO_2 is later quantified by adding a color-forming reagent, sulfanilamide, and analyzed using spectrophotometric techniques.

Under conditions of controlled exposure, the accuracy of the samplers has been demonstrated to be $\pm 10\%$ and precision to be better than 2 ppb for a one-week sampling period (Boleij et al. 1986). Theoretically, under field conditions, over-sampling can be caused by air movements that reduce the transit time of NO_2 molecules along the length of the tube. Under-sampling can occur if the sampling face of the tube is obstructed. Nitrogen dioxide is highly reactive with surfaces and if the samplers are placed in dead-air spaces, surfaces adjacent to the tubes will reduce the NO_2 concentrations and the measured levels will be lower than those in the middle of the room, where the subjects are exposed.

In addition to the physical aspects of placement and use, the accuracy of the tubes also is determined by the accurate measurement of exposure time. The uptake of NO_2 follows Fick's First Law and the average concentration is calculated using a diffusion coefficient of $0.154 \text{ cm}^2/\text{sec}$ and the duration of time that the sampler was open (Boleij et al. 1986):

$$Q = -DC\frac{A}{Z}t$$

where Q is the quantity of transferred NO_2 (mol), D is the diffusion coefficient of NO_2 in air (cm^2/sec), C is the concentration of NO_2 at the open end of the tube (mol/cm^3), A is the cross-sectional area of the tube (cm^2), Z is the length of the tube (cm), and t is the time of exposure of the sampler tube (sec).

RESULTS

In the main study, 5% of the total number of samplers were deployed as duplicates to assess measurement precision. A scatterplot of a random sample of 10% of the 1,975 pairs of samplers placed in bedrooms during 1988 through 1991 is presented in Figure 10. The differences between

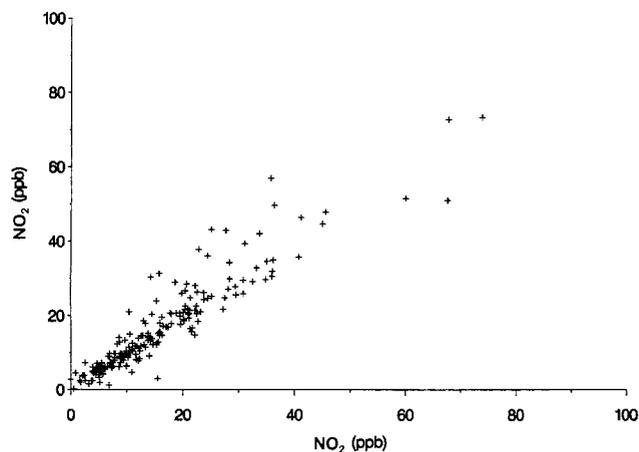


Figure 10. Scatterplot of duplicate NO_2 measurements made by mothers in the main study, 1988 through 1991. For clarity, this scatterplot is based on a random sample of 10% of the total 1,975 duplicate measurements.

pairs of tubes tended to be normally distributed around zero (Figure 11).

In the entire sample of 1,975 duplicates, the median difference was 1.5 ppb, the mean difference was 3.0 ppb, and the standard deviation was 5.8 ppb. Of the duplicates, 95% differed by less than 11.4 ppb and the maximum differ-

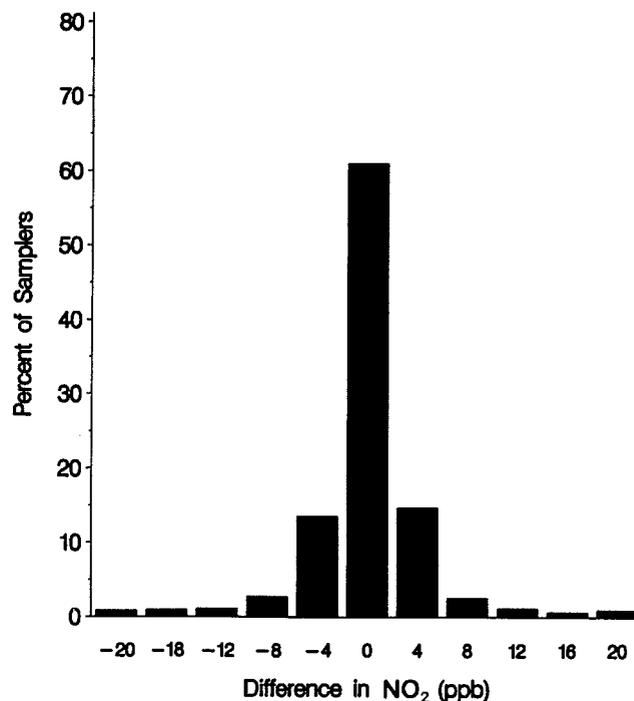


Figure 11. Distribution of differences in duplicate NO_2 measurements made by mothers in the main study, 1988 through 1991, based on a total of 1,957 duplicate measurements.

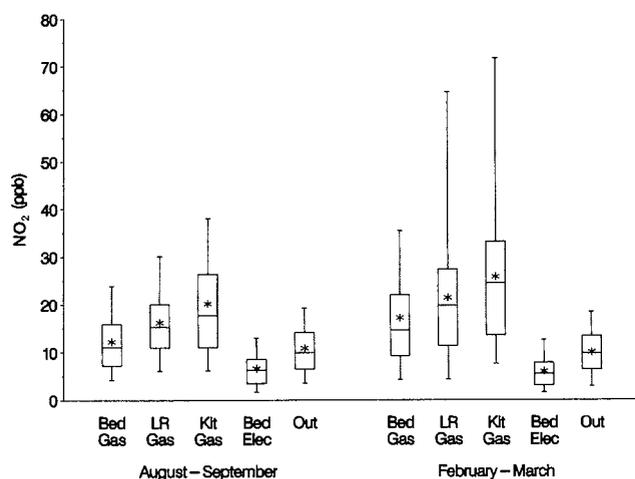


Figure 12. Distributions of NO_2 concentrations measured by samplers placed by technicians, reported by stove type, room, and time of QA and QC survey. The box and whisker plots show the 25th and 75th percentiles as the bottom and top edges of the boxes, respectively. The medians are indicated by horizontal lines and the means by asterisks. The vertical lines extend to the 5th and 95th percentiles of the distributions.

ence was 116 ppb. The Pearson correlation (r) between the paired measurements was 0.92. The more extreme differences in duplicates could not be explained by information routinely collected on the sampler tube use.

Also in the main study, 5% of the sampler tubes were deployed as field blanks. These tubes were never opened and accompanied other sampler tubes through all stages of handling, including being sent to the subjects' homes. Using the deployment times of the tube sets in which the field blanks were included, mean concentration of the 2,388 field blanks was 0.6 ppb ($SD = \pm 4$).

During the August and September survey (summer), mean NO_2 concentrations measured by the technicians' samplers were 12 ppb in the bedrooms, 16 ppb in the living rooms, and 20 ppb in the kitchens (Figure 12). During the second survey in February and March (winter), the room concentrations were higher and averaged 16, 21, and 26 ppb, respectively (Figure 12). Differences in concentrations measured by the technicians and the mothers were more pronounced during the winter survey. Measurements of NO_2 outside the homes averaged 11 ppb in August and September, and 10 ppb in February and March. The mean indoor and outdoor NO_2 concentrations measured during the summer and winter QA surveys were lower than the corresponding seasonal concentrations determined in the main study (Lambert et al. 1993).

During the August and September survey of 214 homes, the overall percentage of compliance was 52% (Table 7). In four homes (2%), the mothers had continued to place the samplers in their own bedrooms although their children

were no longer sleeping there. Relative to the samplers placed by the technician in the index sub bedrooms, the differences in NO_2 concentrations ranged from -1.6 to 1.3 ppb and averaged -0.2 ppb (Table 7). In 24 homes (11%), samplers had been moved by the parents and were judged by the technicians to have been placed in dead-air spaces. In these situations, the difference in measured NO_2 concentrations ranged from -15.8 to 3.9 ppb, and averaged -0.3 ppb. In 27 homes (13%), the proper sampler tubes were not open at the time of the technicians' visits; the delays ranged from hours to eight days, with a median delay in opening of one day. The resulting differences in measured NO_2 concentrations ranged from -2.3 to 12.4 ppb and averaged 0.5 ppb. In 20 homes (6%), sampler tubes were not closed at the time of the technicians' return visits. The differences in measured NO_2 concentrations caused by the delay of closing ranged from -1.6 to 3.0 ppb and averaged 0.1 ppb.

Across the 214 homes for which comparison measurements were obtained during August and September, differences in the bedroom measurements made by the technicians relative to those made by the mothers ranged from -22.9 to 12.4 ppb, with a mean of 0.3 ppb ($SD = 4.0$) (Table 7). No clear trends in measurement error by room were observed (Table 8).

When the homes were revisited in February and March, audit findings were similar to those from August and September (Tables 7 and 8). The slightly higher mean difference and variance in NO_2 concentrations measured by the technicians' samplers relative to those placed by the parents is attributed to higher indoor NO_2 concentrations during the winter. During this second survey, the noncompliance rate was lower, 24 percent, compared with 48 percent in the first survey. Placement of the samplers in dead-air spaces, too close to windows or exterior doors, or with the samplers' open ends up rather than down were less frequently observed in the second QA survey. However, the technicians observed that parents frequently had moved the samplers from the agreed upon locations and had not exchanged the samplers on schedule (Table 9). Of the 176 households participating in both QA surveys, 33% (58/176) were fully compliant in both audits, and 25% (44/176) were noncompliant on at least one criterion on both audits (Table 9).

The impact of noncompliance was further evaluated by pooling the data from the two QA surveys and plotting the distribution of differences in NO_2 measurements made by the technicians and the mothers (Figure 13). For the most common types of deviations from protocol, the range of differences was quite similar to the distribution of differences for samplers that were judged to be properly used (see the "No Problems" category of Figure 13).

The scatterplot and distribution of differences in dupli-

Table 7. Compliance in Placement and Use of Sampler and Comparison of Nitrogen Dioxide Measurements from Samplers Placed by Parents and Technicians^a

Sampler Placement or Use	Number of Homes		Difference in Measured NO ₂ Concentrations (ppb)	
	<i>n</i>	%	Mean ± SD	Range
August and September 1990^b				
Wrong room	4	2	-0.2 ± 1.3	-1.6 to 1.3
Moved sampler	37	17	0.0 ± 4.5	-20.8 to 8.4
Dead-air space	24	11	-0.3 ± 3.5	-15.8 to 3.9
Too close to window or door	19	9	-3.4 ± 7.8	-20.8 to 3.0
Open end up	24	11	0.0 ± 5.1	-20.8 to 7.0
Open late	27	13	1.5 ± 2.8	-2.3 to 12.4
Close late	20	9	0.7 ± 1.2	-1.6 to 3.0
Any problem	102	48	0.5 ± 4.5	-20.8 to 12.4
No problem	112	52	0.1 ± 3.6	-22.9 to 9.9
February and March 1991^c				
Wrong room	2	1	4.9 ± 5.9	0.7 to 9.1
Moved sampler	22	13	-0.7 ± 13.9	-57.0 to 9.7
Dead-air space	2	1	-1.4 ± 1.8	-2.7 to -0.2
Too close to window or door	6	4	-3.7 ± 16.5	-36.6 to 7.4
Open end up	7	4	-5.9 ± 14.0	-36.6 to 3.9
Open late	33	19	1.2 ± 4.6	-8.6 to 23.0
Close late	17	10	1.6 ± 3.8	-2.2 to 13.1
Any problem ^d	41	24	-1.2 ± 11.7	-57.9 to 9.7
No problem	130	76	0.4 ± 4.7	-30.4 to 23.0

^a Based on bedroom NO₂ measurements. Values from samplers placed by parents were subtracted from those placed by technicians.

^b *n* = 214 homes total.

^c *n* = 171 homes total.

^d Homes with one or more discrepancies observed for the bedroom sampler placed by the parent.

cate measurements made by the technicians during the audits are presented in Figures 14 and 15. The distribution of differences was approximately centered at 0 ppb (Figure 15). The variance for the differences in duplicate measurements made by technicians was smaller (Figure 15) than for those made by parents (Figure 11).

DISCUSSION

Quality assurance measurements are obtained using methods that are independent of those routinely used. In this study, QA audits consisted of a home visit by a trained technician to quantitatively assess the mothers' use of the

Table 8. Difference in Nitrogen Dioxide Concentrations Measured by Samplers Placed by Technicians and Parents

Room	<i>n</i>	Difference in Measured NO ₂ Concentrations ^a (ppb)	
		Mean ± SD	Range
August and September 1990			
Bedroom	214	0.3 ± 4.0	-22.9 to 12.4
Living room	43	1.3 ± 3.5	-12.4 to 11.6
Kitchen	44	1.2 ± 3.3	-4.4 to 12.2
February and March 1991			
Bedroom	171	0.0 ± 7.0	-57.0 to 23.0
Living room	18	0.0 ± 3.3	-6.3 to 9.4
Kitchen	16	2.5 ± 7.1	-6.0 to 21.4

^a Values from samplers placed by parents were subtracted from those placed by technicians.

Table 9. Cross-Tabulation of Compliance for Households Participating in Both Quality Assurance Surveys^a

First Survey	Second Survey		
	Compliant	Late Open/Close	Other
Compliant	58	20	9
Late Open/Close	18	10	5
Other	27	16	13

^a Number of homes out of 176 surveyed.

tubes and to place a separate set of samplers in the home to measure NO₂ levels. In these audits, generally low rates of noncompliance were documented, and the differences in NO₂ concentration measured by sampler tubes placed by technicians compared with those placed by mothers averaged less than 1 ppb (Tables 7 and 8; Figure 15).

The most commonly observed problem was delay in exchanging the sampler tubes, which occurred in approximately 7% of homes. A delay in opening or closing a set of tubes would tend to lower or raise the calculated NO₂ concentrations. For example, if the mother did not report a two-day delay in exchanging samplers deployed for 14 days, the calculated NO₂ concentration per day would be 14% low in the tube that remained in place for 16 days and 14% high for the tube that remained in place 12 days (assuming other times of sampler exchange were correctly reported). During training on the use of the sampler tubes at enrollment and later during the course of the study, the importance of accurate reporting of the opening and closing times was

stressed. Mothers were encouraged to inform us if they were unable to exchange the samplers at the time of the phone call; however, we are certain that unreported delays occurred and are a source of variability in the longitudinal series of measurements. The consequences of error in sampler deployment times for estimates of cumulative exposure for a season or throughout the year were expected to be minimal; exposure estimates based on the average of several consecutive samplers also were expected to remain unbiased.

Mothers also moved the passive diffusion samplers from their original placements to areas that the technicians considered to be potential dead-air spaces. These locations included corners of rooms, at the rear of bookshelves, and behind objects on shelves. As would be anticipated, these samplers tended to underestimate room NO₂ concentrations compared with samplers placed in more open areas by the technicians (Figure 13); however, the magnitude of the difference was not large. This result may be explained by the range of low indoor concentrations observed in this study (Samet et al. 1992; Lambert et al. 1993) and the difficulty of identifying dead-air spaces by visual inspection.

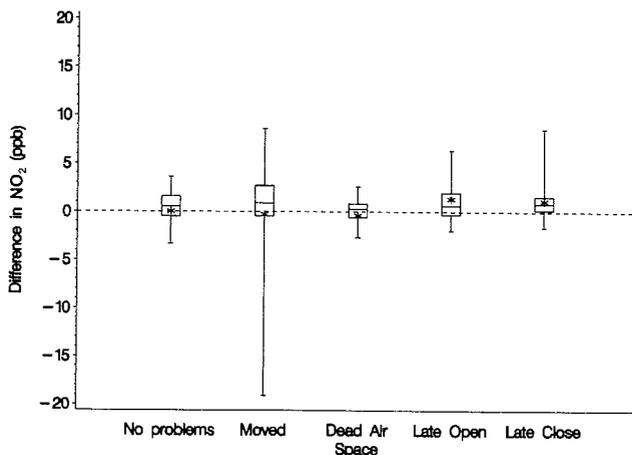


Figure 13. Distributions of differences in NO₂ measurements from samplers placed by technicians and mothers for all samplers by category of misuse. The box and whisker plots show the 25th and 75th percentiles as the bottom and top edges of the boxes, respectively. The medians are indicated by horizontal lines and the means by asterisks. The vertical lines extend to the 5th and 95th percentiles of the distributions.

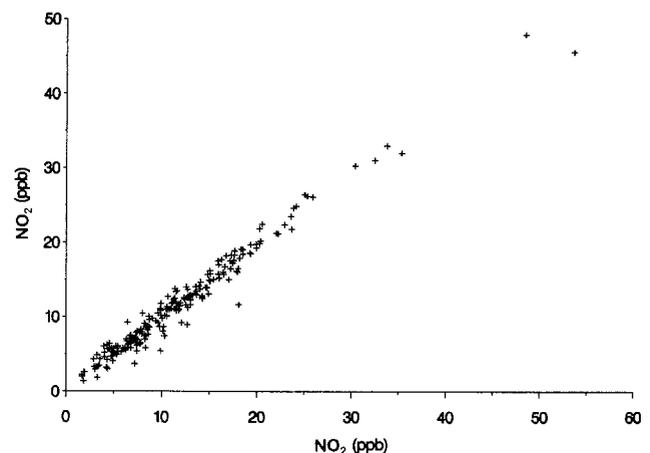


Figure 14. Scatterplot of 214 duplicate NO₂ measurements from samplers placed by technicians in the August and September QA survey.

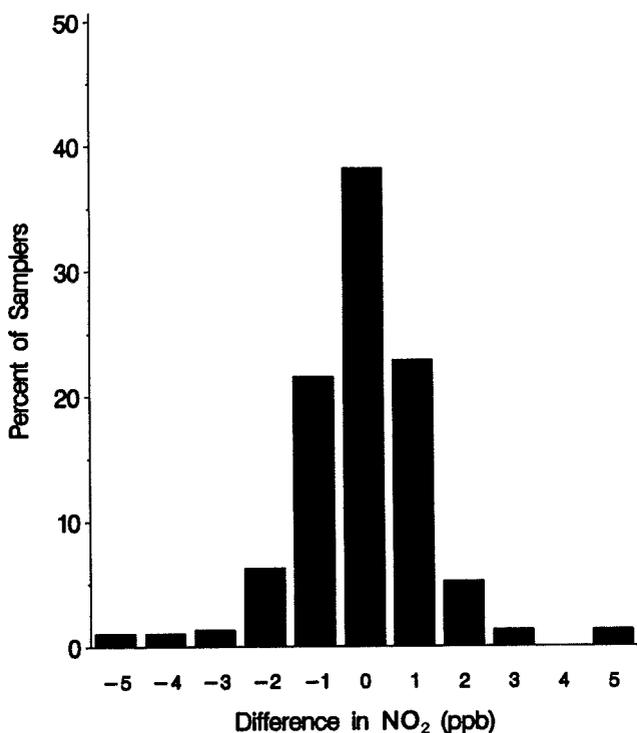


Figure 15. Distribution of differences in 214 duplicate NO₂ measurements from samplers placed by technicians in the August and September QA survey.

The lower rates of noncompliance in the second QA survey among homes that were not in compliance during the first survey (Table 9) imply that corrective actions taken at the end of the first survey were only moderately effective. Fifty-six percent of mothers delayed opening or closing the samplers in both surveys, indicating a chronic problem that persisted in spite of our methods of correction. Across the two QA surveys, the prevalence of delays in opening or closing the samplers was 22%.

In most cases, deviations from protocol did not result in large measurement errors. The errors tended to be distributed symmetrically about the mean. The mean difference was near zero and the standard deviation was relatively small (Table 7), suggesting that the sampler tubes deployed by the parents, although sometimes misused, provided accurate measurements of indoor NO₂ concentrations.

Because of practical constraints, many exposure surveys have relied on research subjects to properly use monitoring devices. Protocols are simplified to ease the burdens and inconveniences associated with the use of monitors; however, even the most highly motivated subjects may not always

comply. In our study, mothers may have intended to exchange sampler tubes immediately after our telephone call but then were distracted by more urgent family matters. Although they later exchanged the samplers, they may not have informed us of the late exchange because of embarrassment or not appreciating the importance of exposure time information for the accuracy of measurements. These omissions occurred despite our efforts to be nonjudgmental about late exchanges and to thank the mothers for correcting our data from the prior telephone call. During the first QA study we asked mothers about problems they may have had with the monitoring protocol. Only two mothers (less than 1%) said that they had often delayed exchanging the samplers; however, these mothers would record the time and later report the correction.

During the course of conducting the main study, we suspected that some parents were not using the passive sampler tubes as intended because of extreme differences observed in some duplicate measurements. However, duplicate measurements provided an incomplete understanding of the subjects' use of the NO₂ samplers. It is conceivable that subjects could properly place samplers in their homes and misuse the duplicates or the duplicates could be incorrectly deployed yet produce comparable measurements. In our study, comparisons of duplicate measurements made by the mothers indicated that most samplers located near each other provided similar measurements of NO₂ concentrations (Figures 10 and 11). These findings are similar to those of another survey of residential NO₂ levels (Ryan et al. 1988) that relied on study participants rather than technicians to deploy samplers.

Because passive samplers are becoming available for many air pollutants and are being more frequently used in exposure surveys in community and occupational settings, issues of misuse and measurement error have become important. The findings of our QA studies indicate that audits are necessary to completely assess the reliability and validity of measurements made by study participants. While the precision of measurements from passive samplers may be evaluated by comparison of duplicate measurements, it should be recognized that this comparison does not provide information on validity. The validity of measurements can only be assessed using audit standards and methods that are different from those routinely used. We recommend that monitoring protocols that rely on independent use of monitors by subjects be periodically evaluated against measurements obtained by technicians. In particular, these audits should be sensitive to the misreporting of opening and closing times of samplers, a problem that appears to be prevalent and, for some applications, may be an important source of measurement error.

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REFERENCES

- American Society for Testing and Materials (ASTM). 1988. Sampling and analysis of nitrogen dioxide content of the at-mosphere (diffusion tube methodology). American Society for Testing and Materials, Philadelphia, PA.
- Bierma TJ, Croke KG, Swartzman D. 1989. Accuracy and precision of home radon monitoring and effectiveness of EPA monitoring guidelines. *J Air Pollut Control Assoc* 39:953-959.
- Boleij JSM, Lebret E, Hoek F, Noy D, Brunekreef B. 1986. The use of Palmes diffusion tubes for measuring NO₂ in homes. *Atmos Environ* 20:597-600.
- Colome SD, Lambert WE, Castaneda N, Baker PE. 1987. Per-formance characteristics of Palmes diffusion tubes used for measurement of nitrogen dioxide outside residential sites. In: *Indoor Air '87: Proceedings of the Fourth International Conference on Indoor Air Quality and Climate, Vol. 1, Volatile Organic Compounds, Combustion Gases, Particles and Fibres, Microbiological Agents* (Seifert B, Esdorn J, Fischer M, Rüden H, Wegner J, eds.) pp. 400-404. Institute for Wa-ter, Soil and Air Hygiene, Berlin, Germany.
- Denny FW, Clyde WAJ. 1986. Acute lower respiratory tract infections in nonhospitalized children. *J Pediatr* 108:635-646.
- Dingle JH, Badger GF, Jordan WSJ. 1964. *Illness in the Home: A Study of 25,000 Illnesses in a Group of Cleveland Families*. Press of Western Reserve University, Cleveland, OH.
- DSK. 1992. Safer home test kit (advertised in Spring 1992 "Right Start Catalog" of products for infants and children). DSK, Westlake, CA.
- Epidemiology Task Group of the Chemical Manufacturer's Association. 1991. *Guidelines for Good Epidemiology Prac-tices for Occupational and Environmental Epidemiologic Research*. Chemical Manufacturer's Association, Washing-ton, DC.
- Epidemiology Work Group of the Interagency Regulatory Liaison Group. 1981. *Guidelines for documentation of epidemiologic studies*. *Am J Epidemiol* 114:609-618.
- Gardner PS. 1986. Immunofluorescence. In: *Clinical Virology Manual* (Spector S, Lancz GJ, eds.). Elsevier Science Publishing Co., New York, NY.
- Gardner G, Frank AL, Taber LH. 1984. Effects of social and family factors on viral respiratory infection and illness in the first year of life. *J Epidemiol Community Health* 38:42-48.
- Graham NMH. 1990. The epidemiology of acute respiratory infections in children and adults: A global perspective. *Epidemiol Rev* 12:149-178.
- Lambert WE, Samet JM, Hunt WC, Skipper BJ, Schwab M, Spengler JD. 1993. *Nitrogen Dioxide and Respiratory Illness in Children: Part II. Assessment of Exposure to Nitrogen Di-oxide*. Research Report No. 58. Health Effects Institute, Cam-bridge, MA.
- Lee K, Yanagisawa Y, Hishinuma M, Spengler JD. 1992. A passive sampler for measurement of carbon monoxide using a solid adsorbent. *Environ Sci Technol* 26:697-702.
- McCarthy JF, Bearg DW, Spengler JD. 1991. Assessment of indoor air quality. In: *Indoor Air Pollution: A Health Per-spective* (Samet JM, Spengler JD, eds.). Johns Hopkins University Press, Baltimore, MD.
- McLaren LC. 1986. Hemagglutination inhibition and he-madsorption. In: *Clinical Virology Manual* (Spector S, Lancz GJ, eds.). Elsevier Science Publishing Co., New York, NY.
- Monto AS, Napier JA, Metzner HL. 1971. The Tecumseh study of respiratory illness: I. Plan of study of observations on syndromes of acute respiratory disease. *Am J Epidemiol* 94:269-279.
- Monto AS, Ross H. 1977. Acute respiratory illness in the

- community: Effect of family composition, smoking, and chronic symptoms. *Br J Prev Soc Med* 31:101-108.
- Monto AS, Ullman BM. 1974. Acute respiratory illness in an American community. *JAMA* 227:164-169.
- Palmes ED, Gunnison AS, Dimaggio J, Tomczyk C. 1976. Personal sampler for nitrogen dioxide. *Am Ind Hyg Assoc J* 37:570-577.
- Ryan PB, Soczek ML, Treitman RD, Spengler JD. 1988. The Boston residential NO₂ characterization study: II. Survey methodology and population concentration estimates. *Atmos Environ* 22:2115-2125.
- Samet JM, Lambert WE, Skipper BJ, Cushing AH, Hunt WC, Young SA, McLaren LC, Schwab M, Spengler JD. 1993. Nitrogen Dioxide and Respiratory Illness in Children: Part I. Health Outcomes. Research Report Number 58. Health Effects Institute, Cambridge, MA.
- Samet JM, Lambert WE, Skipper BJ, Cushing AH, McLaren LC, Schwab M, Spengler JD. 1992. A study of respiratory illnesses in infants and nitrogen dioxide exposure. *Arch Environ Health* 47:57-63.
- Samet JM, Marbury MC, Spengler JD. 1988. Health effects and sources of indoor air pollution: Part I. *Am Rev Respir Dis* 136:1486-1508.
- Samet JM, Marbury MC, Spengler JD. 1988. Health effects and sources of indoor air pollution: Part II. *Am Rev Respir Dis* 137:221-242.
- Samet JM, Spengler JD. 1989. Nitrogen Dioxide and Respiratory Infections: Pilot Investigations. Research Report Number 28. Health Effects Institute, Cambridge, MA.
- Samet JM, Tager IB, Speizer FE. 1983. The relationship between respiratory illnesses in childhood and chronic air-flow obstruction in adulthood. *Am Rev Respir Dis* 127:508-523.
- Samet JM, Utell MJ. 1990. The risk of nitrogen dioxide: What have we learned from epidemiological and clinical studies? *Toxicol Ind Health* 6:247-262.
- Schmidt NJ, Emmons RW, eds. 1989. Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections, 6th ed. American Public Health Association, Washington, DC.
- Shy CM, Goldsmith JR, Hackney JD, Lebowitz MD, Menzel DB. 1978. Health effects of air pollution. *ATS News* 6:1-63.
- SKC. 1993. Comprehensive Catalog and Air Sampling Guide, Winter ed. SKC, Inc., Eighty Four, PA.
- Southern California Gas Company. 1986. Residential Indoor Air Quality Characterization Study of Nitrogen Dioxide: Phase I, Vol. 2, Final Report. Southern California Gas Company, Los Angeles, CA.
- U.S. Environmental Protection Agency. 1976. Quality Assurance Handbook for Air Pollution Measurement Systems: Vol. 1, Principles. EPA-600/9-76-005. Office of Research and Development, Research Triangle Park, NC.
- U.S. Environmental Protection Agency. 1983. Toxic Substance Control Act (TSCA): Good Laboratory Practice Standards, Final Rule. *Fed Reg* 48:53922-53944 (November 29, 1983).
- U.S. Environmental Protection Agency. 1989. Toxic Substance Control Act (TSCA): Good Laboratory Practice Standards, Final Rule. *Fed Reg* 54:34034-34050 (August 17, 1989).
- U.S. Food and Drug Administration. 1987. Good Laboratory Practice Regulations, Final Rule. *Fed Reg* 52:33768-33782 (September 4, 1987).
- Wilson AL, Colome SD, Baker PE, Cunningham SJ, Becker EW, Bope WG. 1987. Comparison of passive and chemiluminescence monitors for determining one-week average nitrogen dioxide concentrations. In: *Indoor Air '87: Proceedings of the Fourth International Conference on Indoor Air Quality and Climate, Vol. 1, Volatile Organic Compounds, Combustion Gases, Particles and Fibres, Microbiological Agents* (Seifert B, Esdorn J, Fischer M, Rden H, Wegner J, eds.) pp. 456-460. Institute for Water, Soil and Air Hygiene, Berlin, Germany.
- Wright AL, Holberg CJ, Martinez FD, Morgan WJ, Taussig LM, Group Medical Associates. 1989. Breast feeding and lower respiratory tract illness in the first year of life. *Br Med J* 299:946-949.

APPENDIX A. Example of a Standard Operating Procedure

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UNM STUDY OF INFANT RESPIRATORY ILLNESS INITIAL HOME VISIT BY FIELD INTERVIEWER

1.0 INTRODUCTION

During the first two months of participation, the baby's home will be visited several times by the Field Interviewer. This initial home visit involves an interview on home structural characteristics and appliances, and the placement of nitrogen dioxide (NO₂) sampler tubes in several rooms. Because this visit is often the respondent's first contact with project personnel, this visit serves to familiarize the parent with the Study's protocols and sets the tone for their cooperation.

1.1 Purpose

During the initial home visit, baseline information will be collected on home factors and occupant behaviors which will influence the baby's residential exposure to NO₂. Locations for the placement of the NO₂ sampler tubes are chosen and the first set of tubes is deployed. Additionally, the Field Interviewer will explain to the parents the kinds of activities that they may expect as participants in the Study. An informed consent is signed by the Field Interviewer and the parent(s).

1.2 Principle of the Method

Data on home characteristics and occupant behavior is collected using a questionnaire, and by walking through the home to examine appliances and to measure the dimensions of the living quarters. According to a set of general guidelines, the sampler tubes are placed in locations around the house away from the influence of indoor sources and absorbers of NO₂.

2.0 RESPONSIBILITIES

The Field Interviewer is responsible for conducting the initial home visit to obtain informed consent, assess housing characteristics and to deploy the first set of NO₂ sampler tubes.

3.0 EQUIPMENT

- (1) Two Consent Forms
- (2) Home Characteristics Questionnaire (Form 2.3)
- (3) Field Technician Survey (Form 2.4)
- (4) Nitrogen Dioxide Sampler Placement Form (Form 2.12)
- (5) Nitrogen Dioxide Sampler Field Card (Form 2.11)
- (6) Business cards
- (7) UNM Photo ID badge
- (8) Clipboard and red ink pens
- (9) Calculator
- (10) Set of Labeled NO₂ Sampler Tubes

- (11) Rack or clips to hold sampler tubes
- (12) Pliers to open sampler tubes
- (13) Tape measure or measurement wheel
- (14) Map to the respondent's home
- (15) City map
- (16) Mileage form

4.0 PROCEDURE

4.1 Preparations

Before leaving the Project Offices for the respondent's home, make certain that you have adequate directions to the home, and that the above listed forms and materials are organized and ready for use. The respondent's name and RID number should be recorded on each form to be used. The UNM Photo ID Badge is to be prominently worn on all home visits. Your dress and appearance should be neat; clothing can be casual, but should always be conservative and professional looking. If using your own vehicle, the starting and ending mileage for the trip should be recorded on the Mileage Form.

4.2 Step-by-step Operations

1. The first task of the Field Interviewer is to give a general explanation of the research study and outline the activities involved in the first home visit. The Field Interviewer should then read the Consent Form to the parent(s) and explain what their participation, and that of their child's, will entail. The mother and the father should understand that their participation, and that of their baby's, is entirely voluntary, and that they may drop out of the Study without penalty at any time. The Consent Form is a legal document. Two copies are to be completed and signed by the parents and the Field Interviewer. One copy is to be left with the baby's parents and the other will be kept in the respondent's file in the Project Office. Special consent forms have been developed for each of the hospitals providing research subjects: University of New Mexico Hospital, Lovelace Medical Center, Presbyterian Hospital, and St. Joseph West Mesa and Heights General hospitals. The consent form corresponding to the subject's location of recruitment should be used.

2. After explaining the Study and obtaining informed consent, the interviewer will administer the Home Characteristics Questionnaire (Form 2.3). This interview requests information on the structural features and age of the residence, and how appliances are used in the home. Based upon answers to this questionnaire, the interviewer will then walk through the home with the mother or father and will examine the appliances and aspects of the house structure.

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3. Information gathered on the walk-through will be recorded on the Field Technician Survey (Form 2.4). Measurement of the dimensions of the living quarters and the distances from the range and the furnace to the baby's bedroom should be completed last and without calling them to the parent's attention.

4. After completion of the Field Technician Survey, place the NO₂ sampler tubes about the inside of the house. In homes with gas ranges, tubes will be placed in the infant's bedroom, the living room or activity room, and the kitchen. In homes with electric ranges, tubes will be placed only in the infant's bedroom. Tubes will be held by metal racks that can stand on the top of tables, cabinets or other furniture. The racks will be placed at locations away from the direct effects of combustion appliances, and away from windows and exterior doors and walls. Tube placement is critical, as the sampler must be located in such a way as to give a representative sample of the pollutant levels in the breathing zone of the baby. The Interviewer should talk over the placement of the racks with the mother to find a convenient location for her which are also out of reach of the baby and his/her siblings. The racks are to remain in these locations over the 18 months of the Study. The parents are to be told not to move the racks. The locations of the tubes and racks is to be recorded on the Nitrogen Dioxide Sampler Placement Form (Form 2.6).

4. After the tubes are placed about the home and opened, record the date and time of opening on the NO₂ Sampler Field Card (Form 2.11).

5. Finally, the Field Interviewer should briefly remind the parents of the use in the research. Usually this will be a home visit by the Nurse to train the mother on the use of the calendar-Diary to record the baby's health symptoms. The Field Interviewer should also make arrangements to telephone the mother in two week's time. When the Interviewer telephones, she will conduct the Health Surveillance and Time-Activity Interviews, and the mother may be asked to cap and uncap some of the sampler tubes. The parents should be thanked for their help and a business card for the Study should be left so that the parents may contact the Project Offices.

4.2.1 NO₂ Sampler Placement Protocols

The nitrogen dioxide (NO₂) diffusion tube samplers used in this study were developed at the University of Wisconsin, Madison by Edward Palmes, and hence the tubes have been called "Palmes tubes". The samplers work by absorbing NO₂ gas molecules from the air. NO₂ molecules move about in the air, propelled by currents (i.e., convective movements of air) and by random motion (i.e., diffusion). The Palmes tube is constructed so that NO₂ molecules can diffuse up the three-inch Plexiglas tube to be absorbed onto screens which have been coated with a chemical

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absorbant. The body of the tube functions to shield these screen from wind currents. Wind currents hitting the screens could deliver more NO₂ to the screens than normally would reach them by passive diffusion. Once absorbed onto the screens, the NO₂ molecules become chemically bound and are not released. As long as the tube is open, it continues to absorb NO₂ from the air. Because NO₂ molecules diffuse up the length of the tube at a constant rate, we can calculate the average amount of NO₂ present in the room if we know how long the tube was open to the air.

(1) Choose a Location for the Sampler Tube: To get representative samples of the NO₂ present in a room, it is critical that the sampler be placed away from (a) dead spaces where the air does not circulate, and (b) away from surfaces which absorb NO₂. Examples of a deadspace are a recess in a bookcase or on a countertop behind objects and under shelving. NO₂ is a reactive gas and can be absorbed or changed by coming into contact with surfaces such as walls and fabric. Therefore, always place the tube several inches out from walls and keep the opening of the tube from direct contact with any surface. The best location for the tubes is in the racks set on top of flat surfaces such as tables, dressers or countertops. The rack should be out away from the wall towards the center of the room. If using alligator clips to place the tube, locate the tube on an object that is out away from the wall.

NOTE: Do not place the tubes directly in front of fans, vents, air conditioners, hot air ducts, or other locations where air is moving quickly. Do not place the tubes next to windows, or doors leading to the outside or into the garage. Do not place the tube near sources of water such as sinks or humidifiers. Do not place the tubes within 6 feet of appliances with open flames (i.e., gas ranges or portable gas/kerosene space heaters).

(2) Hang the Sampler Tube Pointing Downward: To prevent contamination of the tube, hang the tubes downward that dust particles do not drift down onto the absorbing screens. A tiny speck of dust containing nitrogen compounds can falsely increase the NO₂ levels measured by the tubes if it should become absorbed on the screens.

(3) Deploy the Sampler Tube(s): To use the tubes, remove the red cap with the lip on the end. Place the tubes with the open end pointing downward. Keep the opening at least 3/4" away from objects or surfaces. Place the tubes within the breathing zone of the infant, normally 3-6 feet above the floor. Remember to place the tubes in the open where air circulates freely around them, but away from the effects of wind currents such as heater vents and air conditioner ducts, and away from gas ranges and kerosene space heaters. Record the exact placement of the tube(s) on the Nitrogen Dioxide Sampler Placement Form. Record the time of opening (and closing) of the tubes on the Field Card.

4.3 Calculations and Preparation for Data Entry

Before leaving the home, quickly review the Home Characteristics Questionnaire, Field Technician Survey, NO2 Sampler Placement Form, and Field Card for completeness. It is critically important that the respondent name and RID number, and dates and times are entered on each form before you leave the home. Calculation of the square footage of the living area of the home can be completed back at the Project Offices, however, even this calculation is best done in the home in case of a questionable result. All answers should be recorded in indelible red ink.

4.4 Quality Control and Quality Assurance Checks

The Project Coordinator will accompany the Field Interviewers on five percent of home visits to ensure compliance with written protocols. Each week, respondent charts will be pulled at random and the completed questionnaires related to the initial home visit will be reviewed (along with other records contained in the chart). Questionnaire data will be entered with data entry programs which employ range checks. Logical cross-checks will be performed to evaluate data consistency.

5.0 RECORDS

5.1 Data Collected by this Procedure

Informed consent is obtained from the parents. Structural characteristics of the home and occupant behaviors which influence indoor levels of NO2 are assessed. Locations for the placement of the NO2 sampler tubes are established and documented. The measurement of indoor NO2 levels is begun at the residence.

5.2 Record Forms

- (1) Consent Form
- (2) Contact Sheet
- (3) Home Characteristics Questionnaire (Form 2.3)
- (4) Field Technician Survey Form (Form 2.4)
- (5) Nitrogen Dioxide Sampler Placement Form (Form 2.12)
- (6) NO2 Sampler Field Card (Form 2.11)

5.3 Location/Placement of the Forms

All forms are to remain in the respondent's file located in the Project Offices.

6.0 FORMS

- 6.1 Blank Forms
- 6.2 Question-by-Question Specifications

4a. What is the main heating system used in your home?

- Central forced air furnace 1
- Floor furnace 2
- Wall furnace 3
- Gravity furnace 4
- Built-in electrical units 5
- Fireplace 6
- Wood heating stove 7
- Solar 8
- Other, specify _____ 9
- No heat; "none" 0

Most homes will be predominantly heated by one type of system. It is possible that structural additions to the home have added a second built-in furnace unit. The "main" heating system should be the built-in furnace system most frequently used during the heating season. Record data on the secondary heating system below. Classify the heat distribution system according to type:

Central warm air furnace: Heating unit is in a central location, usually a closet or garage, but sometimes outside the home. Warm air is distributed to rooms by a system of ducts and regulators.

Floor furnace: Located in the crawl space under the floor of a home and heat is carried to rooms by a single floor register. This type of heater is not used in slab foundation construction. Also, it is usually located in the center of the home layout, often in or near a central hallway.

Gravity furnace: This furnace is usually built into a closet or wall. The units often have a metal cover which extends a few inches out from the wall surface. Cool air enters into a duct near the baseboard and warm air exits the furnace through a vent near the ceiling. The gravity furnace has no blower fan; the absence of a fan distinguishes the gravity furnace from the wall furnace.

Built-in electrical units: Electrical heating wires may be installed in walls, ceilings or floors to radiate heat into the room. This style of heating system is common in apartments and condominiums. Note: do not classify electric central warm air or wall/floor furnaces under this category.

Wall furnace: Built into a wall, a common type of heater in slab foundation room additions to older home structures. Cool air is taken in at the lower vents and warm air exits through the upper. The wall furnace has a blower fan to circulate air.

Fireplace: Standard fireplaces without modification are to be considered a "fireplace." Wood heating units may be inserted into fireplaces, and when present, the fireplace should then be classified as a wood heating stove.

APPENDIX B. Home Characteristics Questionnaire and Home Visit Medical History

Figure B.1. Home Characteristics Questionnaire

FORM 2.3QXQ (07/22/88) Revision 1 RID _____

BABY'S NAME _____ DATE _____

First Last Mo Day YR

INTERVIEWER ID # _____

QUESTION-BY-QUESTION SPECIFICATIONS
UNM STUDY OF INFANT RESPIRATORY ILLNESS
HOME CHARACTERISTICS QUESTIONNAIRE

1. PERSON INTERVIEWED
- MOTHER 1
 - FATHER 2
 - GRANDMOTHER 3
 - GRANDFATHER 4
 - OTHER, SPECIFY _____ 5

Before I place the air pollution samplers around your home, I would like to ask a few questions that will help us to better understand the indoor air pollution measurements which we will make.

2. About when was your home originally built?
- Since 1980 1
 - 1970 - 1979 2
 - 1960 - 1969 3
 - 1950 - 1959 4
 - Pre 1950 5
 - Don't Know 7

- 3a. Is there a garage or carport attached to the house or apartment?
- Yes 1
 - No 2

Garage or carport includes any shelter for automobile or truck. Even a simple and relatively open awning structure should be considered a carport.

IF YES

- 3b. Do you keep your car in your garage?
- Everyday 1
 - Only occasionally 2
 - Only when weather is cold 3
 - Never 4

If the garage is exclusively used for storage of an inactive automobile (e.g., one that is not used, or not in operable condition), indicate "Never". We are trying to ascertain if the attached garage is regularly used to park and shelter an active vehicle. "Occasionally" is less than every day, but throughout the year.

Wood heating stove: Wood or coal is burned in this type of heating unit. The classic wood-burning stove is the "Ben Franklin" pot-bellied style, although new designs can take a variety of shapes.

Solar: Radiant heat from the sun can be strategically used to heat a home. Heat collection areas are usually located on the home's south face and may be constructed of glass or metal. There are a variety of means of storing heat, including masonry and drums of water. Diverse and creative methods have been devised. There are too many configurations in solar systems to describe in this limited space, but fortunately most home owners who possess a solar system are proud of it and knowledgeable about its workings. They will be able to accurately identify it for you.

Space heater: In some homes, there may be no built-in furnace or the built-in furnace may not be operable, and a space heater will be used as the main heating source. Space heaters are defined as portable heaters of small capacity, only able to heat a limited space or room. (Small heaters built into the walls of bathrooms should be considered space heaters because of their limited capacity.) Write in "space heater" in the "Other" category and complete questions below on space heater use.

4b. Is there a secondary heating system used in your home?

- Central forced air furnace 1
- Floor furnace 2
- Wall furnace 3
- Gravity furnace 4
- Built-in electrical units 5
- Fireplace 6
- Wood heating stove 7
- Solar 8
- Other, specify _____ 9
- No heat; "none" 0

Circle "No heat; 'none'" if there is no secondary source of heating.

5. What fuel is used most for heating your home?
- Utility natural gas 1
 - Electric 2
 - Wood 3
 - Solar 4
 - Bottled, tank or LP gas 5
 - Other, specify _____ 6
 - Don't know 7
 - No heat; "none" 0

Indicate the fuel that accompanies the most commonly used heating appliance.

- 6a. Do you also use a space heater(s)?
- Yes 1
 - No 2

IF YES

6b. How many? _____

Let's talk about the space heater (or one of the space heaters).

6c. What type of fuel does it use?

Electric	1
Natural gas	2
Kerosene	3
Bottled, tank or LP gas	4

Butane/propane fuels are bottled forms of heating gas.

6d. Where is it used?
(CIRCLE FOR EACH ROOM)

Living room	Y	N
Family room/den	1	2
Dining room	1	2
Infant's bedroom	1	2
Other bedroom(s)	1	2
Bathroom(s)	1	2
Other, specify _____	1	2

6e. Is it vented to the outside?

Yes	1
No	2

Verify venting during Field Interviewer Survey and walk-through of home.

(IF A SECOND SPACE HEATER IS USED)

Let's talk about the other space heater.

6f. What type of fuel does it use?

Electric	1
Utility natural gas	2
Kerosene	3
Bottled, tank or LP gas	4

6g. Where is it used?
(CIRCLE FOR EACH ROOM)

Living room	Y	N
Family room/den	1	2
Dining room	1	2
Infant's bedroom	1	2
Other bedroom(s)	1	2
Bathroom(s)	1	2
Other, specify _____	1	2

6h. Is it vented to the outside?

Yes	1
No	2

7a. Do you have a fireplace?

Yes	1
No	2

IF YES

7b. How many fireplaces do you have in your home? _____

4

to increase humidity? Sometimes 2
Never 3

Now I would like to ask you a couple of questions about your cooking stove.

9. What type of cooking ovens do you use?
(CIRCLE FOR EACH OVEN TYPE)

Gas oven	Y	N
Electric oven	1	2
Microwave oven	1	2
Toaster oven	1	2
Other, specify _____	1	2

In this question record the oven appliances only if actually used. Later, on the Field Technician Survey, you will record the range/oven type present, irrespective of whether or not it is actually used.

Classify oven according to type:

A gas oven is defined as a large capacity oven which generates heat by the burning of natural gas. Physically, it is often part of a range appliance, but also may be configured as a structurally separate unit (e.g., built-in). Similarly, the electric oven is of large capacity but uses electric coils to generate heat.

A microwave oven uses long wave radiation (microwave) to heat food. These units are most often countertop size, but may be built-in.

A toaster oven is a very limited capacity oven in which small-sized food items may be heated (e.g., toast or frozen foods). It is always countertop-sized.

Another type of countertop oven which may be encountered is the convective oven, which is larger than the typical toaster oven. It uses electric heating coils and fans to cook and brown foods. Specify "convective" in the other category. If a combination microwave/convection oven, classify as a "microwave".

10a. Is there an exhaust fan over or near the cooking stove?

Yes	1
No	2

IF YES

10b. Do you usually use the exhaust fan above your stove when cooking?

Always or almost always, whenever stove is on	1
At least half the time the stove is on	2
Occasionally (when kitchen is smokey or for odors)	3
Rarely or never	4

6

7c. In what room(s) is the fireplace(s) located?
(CIRCLE FOR EACH ROOM)

Living room	Y	N
Family room/den	1	2
Dining room	1	2
Infant's bedroom	1	2
Other bedroom(s)	1	2
Other, specify _____	1	2

7d. How often do you use your fireplace(s) during the heating season?

Never	1
Less than once per week	2
One to three times per week	3
Four to six times per week	4
Daily	5

The Albuquerque heating season is defined as the period October through March.

8a. Do you have a wood-burning heating stove?

Yes	1
No	2

IF YES

8b. How many heating stoves do you have in your home? _____

8c. In what room(s) is the heating stove located?
(CIRCLE ALL THAT APPLY)

Living room	1
Family room/den	2
Dining Room	3
Infant's bedroom	4
Other bedroom(s)	5
Other, specify _____	6

8d. How often do you use your wood heating stove(s) during the heating season?

Never	1
Less than once per week	2
One to three times per week	3
Four to six times per week	4
Daily	5

8e. Do you burn fuels other than wood in your heating stove(s)?

Yes	1
No	2

IF YES, specify _____

Less commonly burned fuels include coal, artificial logs made of tightly rolled newspaper. If encountered, specify these alternative fuels.

8f. Do you put pans of water on your stove Always 1

5

11a. Are there windows or exterior doors in the kitchen or cooking area?

Yes	1
No	2

IF YES

11b. Do you open your kitchen windows when cooking?

Always or almost always, whenever stove is on	1
At least half the time stove is on	2
Occasionally (when kitchen is smokey or for odors)	3
Rarely or never	4

12. During the heating season, do you ever use the range or oven to heat your kitchen or home?

Yes	1
No	2

Now, let's talk about some other appliances in your home.

13a. Are water heaters located inside the living area of the residence?
(INCLUDE SERVICE PORCH, ATTACHED GARAGE, OR BASEMENT)

Yes	1
No	2

IF YES

13b. How many? _____
Where? _____

14a. Do you have a clothes dryer?

Yes	1
No	2

IF YES

14b. Is the clothes dryer located inside the living area of the residence?
(INCLUDE SERVICE PORCH, ATTACHED GARAGE, OR BASEMENT)

Yes	1
No	2

IF YES, where? _____

15. What kind of cooling equipment do you use in your home? (CIRCLE FOR EACH ROOM)

Swamp cooler - central unit	Y	N
Swamp cooler - room units	1	2
Refrigerated air - central unit	1	2
Refrigerated air - room units	1	2
Fans	1	2
Do not have cooling equipment	1	2

16. Do you regularly use (ONCE PER WEEK) a humidifier or vaporizer in your home?

Yes	1
No	2

IF YES

7

12a. Did the baby ever have a fever during this illness? WC: Did the baby have a fever in the past three days?

Yes	1
No	2
Don't Know	7

IF YES

12b. How high did the fever get? _____°F

12c. How did you take the temperature?

Rectal	1
Axillary (armpit)	2
Subjective	3

13. Has the illness interfered with eating?

WC: In the past three days has the baby vomited or refused to eat?

Yes	1
No	2

IF COUGH

14. Has the cough interfered with the baby's sleeping?

Yes	1
No	2
N/A	8

3

16d. Did the doctor prescribe any medicine for your baby? (ASK TO SEE BOTTLE AND RECORD)

Yes	1
No	2
N/A	8

IF YES

What was the name of the medicine?

16e. Was a chest x-ray done?

Yes	1
No	2
N/A	8

17. Is your baby taking any (other) medicine?

Yes	1
No	2

PRESCRIPTION MEDICATIONS:

5

15. Did the baby show other signs of being ill? WC: Did the baby show any signs of being ill in the past three days?

Yes	1
No	2

IF YES, specify _____

16a. Did your baby go to the doctor for these symptoms? WC: Did your baby go to the doctor because of illness in the last three days?

Yes	1
No	2

IF YES

16b. What was the date of the visit and the doctor or hospital?

Date: _____

Name of Doctor or Hospital: _____

16c. What did the doctor say was wrong with your baby? (RECORD EXACT STATEMENT)

4

OVER-THE-COUNTER MEDICATIONS:

18. In the week before the baby got sick, did the baby go to the doctor for immunizations? WC: Did the baby go to the doctor for immunizations in the past week?

Yes	1
No	2
DK	7

19. In the week before baby got sick, did any member of the household have:

6

WC: In the past week, did any member of the household have:

(PUT 0 IF NO. PUT NUMBER WITH SYMPTOMS IF YES.)

A cold or sore throat _____
 Cough _____
 Trouble breathing (or pneumonia) _____
 Hoarseness (or laryngitis) _____
 Earache or ear infections _____
 Fever _____
 Other respiratory or health problem _____
 Describe _____

20. Before your baby got sick, did she/he have any contact with anybody else who was sick? Yes 1
 WC: In the past week did she/he have any contact with someone else who was sick? No 2
 DK 7

If so, who was it? _____

What was the illness? _____

21. In the week since your baby became ill,

7

25. Irritable 1 2 3 8
 26. Other, specify 1 2 3 8

B. RESPIRATORY RATE AND PULSE

27. Respiratory rate

Breaths/minute	SLEEPING	QUIET	ACTIVE	CRYING
a. _____	1	2	3	4
b. _____	1	2	3	4
c. _____	1	2	3	4

28. Pulse

Beats/minute	SLEEPING	QUIET	ACTIVE	CRYING
	1	2	3	4

did any member of the household develop:
 (PUT 0 IF NO. PUT NUMBER WITH SYMPTOMS IF YES.)
 (IF WELL CHILD VISIT, DO NOT ASK THIS QUESTION)

A cold or sore throat _____
 Cough _____
 Trouble breathing (or pneumonia) _____
 Hoarseness (or laryngitis) _____
 Earache or ear infections _____
 Fever _____
 Other symptoms _____
 Describe _____

II. PHYSICAL EXAMINATION

A. APPEARANCE

	PRESENT	ABSENT	UNCERTAIN	N/A
22. Alert	1	2	3	8
23. Responsive	1	2	3	8
24. Playful	1	2	3	8

8

a. _____	1	2	3	4
b. _____	1	2	3	4
c. _____	1	2	3	4

C. EYES

	PRESENT	ABSENT	UNCERTAIN	N/A
29. Conjunctive red	1	2	3	8
30. Eye discharge, watery	1	2	3	8
31. Eye discharge, purulent	1	2	3	8

D. NOSE

	PRESENT	ABSENT	UNCERTAIN	N/A
32. Congestion	1	2	3	8
33. Nasal discharge, watery	1	2	3	8
34. Nasal discharge, purulent	1	2	3	8

10

35. Nasal flare	1	2	3	8
E. COUGH				
36. Dry	1	2	3	8
37. Wet	1	2	3	8
38. Frequency of cough during the exam	Frequent ≥5	Infrequent <5	Absent	8
F. HYPOPHARYNX/LARYNX				
39. Inspiratory stridor	1	2	3	8
40. Hoarseness	1	2	3	8
41. Other, specify _____	1	2	3	8

11				

49. Wheezes (W)	1	2	3	8		
50. Rhonchi (RH)	1	2	3	8		
J. TEMPERATURE AND OXIMETRY						
51a. Temperature:	_____°F					
51b. Method of measuring temperature?	Rectal	1				
	Axillary (armpit)	2				
52. Oximetry						
	% of O ₂	Pulse	SLEEPING	QUIET	ACTIVE	CRYING
	Saturation	(BPM)				
a. _____	_____	_____	1	2	3	4
b. _____	_____	_____	1	2	3	4
c. _____	_____	_____	1	2	3	4
13						

G. NECK				
42. Lymph nodes palpable	1	2	3	8
43. Use accessory muscles	1	2	3	8
H. CHEST				
44. Retractions	1	2	3	8
45. Increased A-P diameter	1	2	3	8
46. Prolonged expiratory phase	1	2	3	8
I. LUNGS				
	PRESENT	ABSENT	UNCERTAIN	N/A
47. Breath sounds normal (BS)	1	2	3	8
48. Rales (RA)	1	2	3	8
12				

K. THROAT				
	PRESENT	ABSENT	UNCERTAIN	N/A
53. Lesions	1	2	3	8
Location: _____				
54. Tonsillar exudate	1	2	3	8
L. EARS				
PERFORM TYMPANOMETRY.				
	LEFT EAR		RIGHT EAR	
Canal volume	55a. _____		56a. _____	
TM Compliance	55b. _____		56b. _____	
Middle ear pressure	55c. +/- _____		56c. +/- _____	
Tympanometry diagnosis	55d. Normal 1 Abnormal 2		56d. Normal 1 Abnormal 2	
14				

Inconclusive	3		Inconclusive	3
Artifact	4		Artifact	4
Not performed	8		Not performed	8

57. Tympanometry performed at:

Rest	1
Active	2
Crying	3
Other, specify _____	4

IF TYMPANOGRAM IS ABNORMAL, PERFORM PNEUMATIC OTOSCOPY.

	Yes	No	N/A
58. (R) TM visualized	1	2	8
59. (L) TM visualized	1	2	8
60. (R) TM compliant	1	2	8
61. (L) TM compliant	1	2	8
62. (R) TM red	1	2	8
63. (L) TM red	1	2	8

15

65. Impression of severity:

0 1 2 3 4 5 6 7 8 9 10

WELL	MILD	SEVERE
		(Hospitalization required)

66. Nasal wash performed? Yes 1
No 2
N/A 8

COMMENTS: _____

17

OTHER CONCERNS:

64. Impression of the child's health:

(THE MULTIPLE DIAGNOSIS OF LRI ACCOMPANIED BY URI CAN BE MADE)	WELL	1
	ILL, NOT RESPIRATORY	2
	ILL, UPPER RESPIRATORY	
	SEROUS OTITIS	3
	OTITIS MEDIA	4
	URI, NOT OTHERWISE SPECIFIED	5
	LOWER RESPIRATORY	
	CROUP	6
	(Inspiratory stridor, hoarseness, dry cough)	
	BRONCHIOLITIS	7
	(Wheezing, prolonged expiratory phase, and air trapping)	
	PNEUMONITIS	8
	(Rales, tachypnea, fever)	
	TRACHEOBRONCHITIS	9
	(Wet cough and rhonchi)	
	LRI, NOT OTHERWISE SPECIFIED	10

16

QUALITY ASSURANCE CHECK

1. NO ₂ SAMPLER TUBE(S) IN PLACE IN BABY'S BEDROOM?	Yes	1
	No	2
	N/A	9
1b. NO ₂ SAMPLER TUBE(S) OPEN?	Yes	1
	No	2
	N/A	9
2a. SYMPTOM CALENDAR-DIARY BEING USED BY MOTHER?	Yes	1
	No	2
	N/A	9
2b. CALENDAR-DIARY COMPLETED TO WITHIN LAST 2 DAYS?	Yes	1
	No	2
	N/A	9

RECOMMENDED CORRECTIVE ACTION: _____

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William E. Lambert, the Project Coordinator for the University of New Mexico Study of Infant Respiratory Illness, is Research Assistant Professor in the Department of Family and Community Medicine. He is completing his Ph.D. degree at the University of California, Irvine, in the Department of Environmental Analysis and Design, School of Social Ecology. His research interests have focused on assessment of exposure to air pollutants and the measurement of health effects in the community setting.

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PUBLICATIONS RESULTING FROM THIS RESEARCH

Samet JM, Utell MJ. 1990. The risk of nitrogen dioxide: What have we learned from epidemiological and clinical studies? *Toxicol Ind Health* 6:247-262.

Samet JM, Lambert WE. 1991. Epidemiologic approaches for assessing health risks from complex mixtures in indoor air. *Environ Health Perspect* 95:71-74.

- Samet JM, Utell MJ. 1991. The environment and the lung: Changing perspectives. *JAMA* 226:670-675.
- Lambert WE, Samet JM, Dockery DW. 1992. Community air pollution. In: *Environmental and Occupational Health*, 2nd ed. (Rom WN, ed.). Little, Brown & Co., Boston, MA.
- Lambert WE, Samet JM, Stidley CA, Spengler JD. 1992. Classification of exposure to residential nitrogen dioxide. *Atmos Environ* 26A:2185-2192.
- Samet JM, Lambert WE, Skipper BJ, Cushing AH, McLaren LC, Schwab M, Spengler JD. 1992. A study of respiratory illnesses in infants and nitrogen dioxide exposure. *Arch Environ Health* 47:57-63.
- Lambert WE, Samet JM, Hunt WC, Skipper BJ, Schwab M, Spengler JD. 1993. Nitrogen Dioxide and Respiratory Illness in Children: Part II. Assessment of Exposure to Nitrogen Dioxide. Research Report Number 58. Health Effects Institute, Cambridge, MA.
- Lambert WE, Samet JM, Skipper BJ, Cushing AH, Hunt WC, Young SA, Schwab M, Spengler JD. 1993. Residential exposures to nitrogen dioxide and respiratory illnesses in infants. In: *Indoor Air '93: Proceedings of the Sixth International Conference on Indoor Air Quality and Climate*, Vol. 1, Health Effects (Jaakkola JJK, Ilmarinen R, Seppänen O, eds.). Laboratory of Heating, Ventilating, and Air Conditioning, Helsinki University of Technology, Espoo, Finland.
- Samet JM, Cushing AH, Lambert WE, Hunt WC, McLaren LC, Young SA, Skipper BJ. 1993. Comparability of parent reports of respiratory illnesses with clinical diagnoses in infants. *Am Rev Respir Dis* 148:441-446.
- Samet JM, Lambert WE, Skipper BJ, Cushing AH, Hunt WC, Young SA, McLaren LC, Schwab M, Spengler JD. 1993. Nitrogen Dioxide and Respiratory Illness in Children: Part I. Health Outcomes. Research Report Number 58. Health Effects Institute, Cambridge, MA.
- Samet JM, Lambert WE, Skipper BJ, Cushing AH, Hunt WC, Young SA, McLaren LC, Schwab M, Spengler JD. 1993. Nitrogen dioxide and respiratory illnesses in infants. *Am Rev Respir Dis* 148:1258-1265.
- Schwab M, Spengler JD, McDermott A, Samet JM, Lambert WE. 1993. Seasonal and yearly patterns of indoor nitrogen dioxide levels: Data from Albuquerque, New Mexico. In: *Indoor Air '93, Proceedings of the Sixth International Conference on Indoor Air Quality and Climate*, Vol. 3, Combustion Products, Risk Assessment, Policies (Jantunen M, Kalliokoski P, Kukkonen E, Saarela K, Seppänen O, Vuorelma H, eds.). Laboratory of Heating, Ventilating, and Air Conditioning, Helsinki University of Technology, Espoo, Finland.
- Spengler JD, Brauer M, Samet JM, Lambert WE. 1993. Nitrous acid in Albuquerque, New Mexico, homes. *Environ Sci Technol* 27:841-845.
- Schwab M, Spengler JD, McDermott A, Samet JM, Lambert WE. 1994. Seasonal and yearly patterns of indoor nitrogen dioxide levels: Data from Albuquerque, New Mexico. *Indoor Air* 4:8-22.

ABBREVIATIONS

NO ₂	nitrogen dioxide
ppb	parts per billion
QA	quality assurance
QC	quality control
UNM	University of New Mexico

RELATED HEI PUBLICATIONS: NITROGEN DIOXIDE AND RESPIRATORY DISEASE

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