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Demonstration of Low Cost, Low Burden, Exposure Monitoring Strategies for Use in Longitudinal Cohort Studies

Volume 1 – Final Report

by

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Notice

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Abstract

The Federal Government is currently planning a large, prospective birth cohort study known as the National Children's Study that will potentially involve 100,000 children and their families. The observation period will start as close to conception as possible and will continue for 20 years after birth. Given the magnitude and expense of such a large study, sample collection methods that are amenable to acquisition of samples exclusively by the participants themselves followed by direct shipment to the analysis laboratory present a cost-effective alternative to technician-based sampling procedures. In this pilot study, the ability of participants in three age cohorts to collect environmental and biological samples according to prescribed protocols was evaluated. The cohorts consisted of parents and their children in the ages of 0-1 year, 3-5 years, and 6-8 years old. Biological and environmental samples collected during the study included urine, hair, saliva, breast milk, duplicate diet, tap water, vacuum cleaner dust, floor surface dust wipes, air samples, cotton sock dosimeters, and humidity/temperature measurements. Sample collection instructions and materials were prepared, subjected to evaluation and modification using a test population, and shipped to participants over a 12-month period. Participants were requested to collect the samples, complete questionnaires, and return the samples to the laboratory within defined time periods. Upon receipt at the laboratory, the condition of the samples was assessed by visual inspection and the details of the receipt and evaluation were logged into a computer database; queries were subsequently used to assess compliance. In some cases, chemical analysis was used to further evaluate sample integrity.

The demonstration studies generated considerable information that favorably supports sample collection by study participants and remote data collection via the web, although the studies brought forward a number of issues that can impact a large-scale study such as the NCS. Completion rates for the different on-line surveys were 73% or better. For a relatively complex survey including pesticide use, the response rate was 92%. There was a 96% response rate for completion of a time/activity diary related to the participant child's exposure to pesticides in the home. Participant compliance with sample collection instructions appeared to be good for most sample types. One hundred percent of the hair samples and vacuum cleaner dust samples, for example, were considered to be acceptable. Acceptability rates were greater than 85% for breast milk, urine and food. But the number of acceptable beverage (diet) and tap water samples was lower due to return of leaking containers. The number of acceptable samples was substantially lower for the more complex sampling methods. All of the VOC air sampling badges were returned to the laboratory, but only 56% of the samples were determined to be acceptable. Although an instructional video was included with the badge, the participants found the sample collection method to be too complex. Samples were generally returned in a timely manner, in compliance with the instructions. Results of this project are very encouraging, indicating that remote data collection by study participants is feasible. Results can be used to develop strategies that will maximize completeness of sample collection while minimizing participant burden and study costs.

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Executive Summary

The federal government is planning a large prospective birth cohort study known as the National Children's Study that will potentially involve 100,000 children and their families. The observation period will start as close to conception as possible and follow-up will last for 20 years after birth. There are substantial challenges, both technical and logistical, associated with successfully implementing a study of this magnitude. This demonstration project conducted for U.S. EPA, which is working with NICHD, CDC, and NIEHS in planning the NCS, consisted of a set of pilot studies that involved nine participants in three cohorts. The cohorts included parents and their children in the ages of 0-1 years, 3-5 years, and 6-8 years old. These demonstration studies were designed to address some of the problems that can be anticipated in carrying out the NCS. Our aim was to evaluate the use of data collection methods that impose a minimal burden on the study participants while maintaining high data quality. Broad study objectives included:

- assessing the feasibility of recruiting and retaining study participants (children and their caretakers) in a set of longitudinal exposure studies,
- assessing the feasibility of employing readily available and easy to use sampling methods, instruments, and/or techniques, and
- demonstrating the feasibility of remote data collection methods with readily available, easy to use, state-of-the-art methods, instruments, and techniques for assessing human exposures to environmental contaminants.

Readily-available and commonly used methods, instruments, and techniques were tested over a 12-month data collection period. Selected exposure data (meta data, environmental samples, and biological samples) were collected periodically from participants who were enrolled from an existing web-based panel. A primary objective of the study was to assess the feasibility of remote (home) data collection using a web-based panel. The web is likely to be an important avenue of communication and data collection for the NCS. We assessed the feasibility of using the Internet for providing instructions to participants who collected their own samples and completed questionnaires on-line. The selection of sample types was based on the desire to capture and evaluate an array of typical methods and not to provide data for an actual exposure

study. Biological and environmental samples collected included:

- Cohort: urine, breast milk or duplicate diet (food and beverage);
- 3-5 Cohort: urine, cotton socks, hair, vacuum dust, and tap water; and
- 6-8 Cohort: saliva, dust wipe, volatile organic compounds, and humidity/temperature.

Key Findings for the 0-1 Cohort

We started data collection with 3 breast feeding and 6 non-breast feeding participants. Approximately 45 % of the eligible families that were approached to participate agreed to enroll. There were 6 of 9 participants still returning samples at end of the study. Participants dropping out of the study came from the low and middle income groups. We observed a 73%+ rate for completing metaquestionnaires, which included a food diary, and providing samples. The majority of samples with the exception of the beverage were in good condition when they were received in the lab. Acceptability rates were 85%+ for breast milk, urine, and food; only 69% of the beverage samples were acceptable. Many were unacceptable because they were warm or leaking or the date was not recorded. The study provided evidence that breast milk can be collected without major difficulties. Participants were timely in collecting samples after kits were sent (at least 80% of the samples were collected within 7 days of receiving the kits). An important aspect of the demonstration studies was to determine the extent to which study subjects complied with the instruction of dating samples and completing metaquestionnaires *after* collecting the samples. Participants were remarkably compliant with these instructions. Of all the samples collected, 94% were labeled with a collection date. Of those samples with sample collection and questionnaire completion dates, 96% of the participants completed metaquestionnaires within 1 day of collecting the sample. There were no significant problems completing the metaquestionnaire and food diaries although additional analyses of the data may be appropriate.

The data and samples returned, as well as the results of the quality assurance field visits and calls, indicated that study subjects can successfully collect samples if carefully instructed. A description of the data and sample collection activities is provided in ***Exhibit ES-1***. While none of the activities appeared to be overly burdensome, the retention rate of 66% which was observed for a 12-month study period, might be an important consideration in designing and implementing the NCS.

Exhibit ES-1. Observations on Level of Burden: 0-1 Cohort

Sample/ Data Collection	Description of Activity	Duration[1] (min)	Level of Difficulty[2]	Participant Comments
Breast Milk	Breast pump provided. One 2-oz sample per month requested. Label sample and store in freezer. Disassemble pump and wash. Package sample for shipment.	10	3	One participant indicated that the pump would not work and it was assembled incorrectly.
Food & Beverage	Collect a second portion of all food and beverage consumed by infant in provided containers for each type of sample. Label sample, store in refrigerator through 12-hour collection period, then freeze. Package sample for shipment.	13 (duplicate diet only) 30[3] combined	1	Three-fourths of the participants thought it was "easy" to prepare the duplicate food sample.
Urine	Urine sample collected on gauze pad (inserted into diaper) that is worn the evening after the day the breast milk sample is collected. Pad from feces-free diaper is placed in provided container, which is stored in freezer until shipped. Blue ice is shipped with urine sample.	5[3]	2	Most participants did not find the urine pad collection to be burdensome.
MetaQx and Food Diary	Questionnaire and food diary are to be completed day after samples are collected using WebTV.	10	4	About one-half of participants thought the food diary was "difficult" to "very difficult" to complete.

[1] Average duration of time (in minutes) to complete sample activity as reported by sample participants during debriefing, unless otherwise noted.
[2] RTI estimate of level of difficulty; Scale of 1 – 5, with 1 = easy and 5 = difficult.
[3] RTI estimate of duration

Key Findings for the 3-5 Cohort

The data collection period for the 3-5 year old cohort started with nine participants, but the recruitment rate for this cohort was low. Of the eligible families contacted, only 30% agreed to participate, but the retention rate was very good. Only one participant from the low income strata dropped out, mid-way through the study. Response rates for completing the metaquestionnaires for each of the monthly sampling events (e.g., urine and socks, vacuum dust and hair, and tap water) were very good (~90% or better). Supplemental video instructions were prepared for hair collection. Participants were also generally compliant with providing samples (85%+). Parents of this cohort were successful in returning samples that were suitable for analyses (88%+). Exceptional assistance was obtained in recording the date on the sampling packages (97%+) and completing the metaquestionnaires shortly after the sample was collected (94%+). For the 3-5 cohort, the timeliness for sample collection ranged from 77% for urine to 85% for socks and hair. We received feedback during the quality assurance interviews and the debriefing survey about vacuum dust collection. One participant stated that it was a big problem to collect the vacuum dust sample. Tap water was a relatively easy sample to collect, although we found that several samples were leaking when received in the lab. The level of burden associated with completing the metaquestionnaires and collection of the samples for the 3-5 cohort appears to have been acceptable (***Exhibit ES-2***). All of the metaquestionnaires could be completed relatively quickly (10 minutes or less) and the samples generally took less than 10 minutes to collect, with the exception of the socks which were to be worn for 2 hours.

Key Findings for the 6-8 Cohort

Retention of participants in the 6-8 year old study was very good with eight of nine families continuing to provide data and samples in the last study month. However, recruiting study subjects was marginally successful in that only 31% of the eligible families agreed to participate. The one study subject not completing the study was from the low income strata. Response rates for completing the metaquestionnaires (94%+) and providing samples (94%+) were very good. However, the samples collected by this cohort, notably saliva, VOCs, and HOBO temperature data collection, were in many instances unacceptable for analyses in the lab. Also, we noted that for many of the sample types, the samples were not collected in a timely manner (29% to 69% collected within the specified time period). Parents and children were very

Exhibit ES-2. Observations on Level of Burden: 3-5 Cohort

Sample/ Data Collection	Description of Activity	Duration[1] (min)	Level of Difficulty[2]	Participant Comments
Urine	Collect first morning urine void in specimen cup. Label sample with date and time, as well as the time of last urination. Store in freezer for 24 hours. Package sample for shipment.	3	2	Participants indicated that it was not a problem to collect the first morning urine from their child.
Socks	Wear socks indoors without shoes for 2 hours, and then place in sample container. Freeze overnight. Package sample for shipment.	3	2	Five of the eight study participants or 63% indicated that it was a small problem for them to get their child to wear the socks for a 2-hour period. The remaining three indicated it was not a problem. One child indicated the socks were itchy.
Hair	Cut a 1-inch section of hair from the scalp of the child (instructional video provided). Place in bag and record date and time. Package sample for shipment.	4	4	Only one participant said that it was a problem to collect the hair sample; most said it was not a problem.
Vacuum Dust	Remove vacuum cleaner bag from vacuum and place in plastic bag. Record date and time on label. Package sample for shipment.	7	2	One participant used a vacuum cleaner with a water filtration system. This participant was individually instructed on how to collect a sample of dust from the vacuum.
Tap Water	Fill bottle to red line with tap water from kitchen sink tap. Test pH of water with pH strip. Record the pH, date and time on the label. Store in refrigerator until shipped. Package sample for shipment.	6	1	No problems noted.
MetaQx and Sock Activity Diary	Questionnaire and sock diary are to be completed day after samples are collected using WebTV.	10	3	Participants were able to provide information for each component of the diary; item nonresponse was negligible. Error messages were mentioned by some participants.

[1] Average duration of time to complete (in minutes) sample activity as reported by sample participant during debriefing; unless otherwise noted.

[2] RTI estimate of level of difficulty; Scale of 1 – 5, with 1 = easy and 5 = difficult.

[3] RTI estimate of duration

willing to provide saliva samples (97% response rate); however, few of the samples collected were acceptable for analysis (23%). These problems included no recorded collection date, sample contained mouthwash, or an insufficient collection volume. Collection of dust wipe samples did not present many problems but some were considered unacceptable for analyses because participants did not record the collection date or because very little dust was present. Even though the collection rate for VOC samples was 100%, use of the VOC sampling device was a problem for participants. Only 56% of the samples were acceptable for conducting analyses. We anticipated problems with this sample type and developed a video. Unfortunately, the video was not as accessible via the web as intended. We suspect that one-half of the VOC sampling badges were not worn for the entire 48-hour collection period. The 42-day HOBO temperature collection was also not as successful as anticipated. This type of sample gave some problems that appear to be instrument-related as well as compliance-related.

We noted a problem with the metaquestionnaires for this cohort regarding questions in which respondents were required to account for time over a 24-hour period. There were instances in which the participants had difficulties in accounting for and summing time over a 24-hour period. Cognitive testing and modifications in the web-based study instrument should help to alleviate this kind of problem in future data collection efforts. The burden placed on the study subjects was considered to be reasonable even though participants were asked to provide a variety of samples and metadata (***Exhibit ES-3***). Based on the debriefing data and the quality assurance visits and calls, we confirmed what we saw in the lab, that the VOC badge and saliva sample collection may have imposed a level of burden and difficulty that was greater than that for the other samples.

The demonstration studies generated considerable information, that favorably support sample collection by study subjects and remote data collection via the web, although the studies brought forward a number of issues that can impact a large-scale study such as the NCS and deserve additional consideration. Many of these issues can be handled through, for example, additional cognitive testing to address meta data collection issues, oversampling to compensate for potential drop out rates and compliance issues, alterations in the manner in which samples are shipped, and a recognition of physical limitations that could make sample collection troublesome for some participants, e.g., reading colors on pH strips. Potential limitations of participants should be taken into account. Other issues relate to the sample collection/monitoring methods that can be realistically fielded, given that the participants themselves are to collect samples.

Exhibit ES-3. Observations on Level of Burden: 6-8 Cohort

Sample/ Data Collection	Description of Activity	Duration[1] (min)	Level of Difficulty[2]	Participant Comments
Dust Wipe	Using the template and wet wipe provided, collect dust wipe sample. Record date and time on label. Store in freezer for until shipment. Package sample for shipment.	7	2	Participants noted it was not a problem to collect the dust sample or to place it in the special shipping container.
Saliva	Rinse mouth with mouthwash. Discard used mouthwash. Collect saliva in cup and fill to red line. Record date and time on label. Store in freezer until shipment. Package sample for shipment.	10	2	Four of the participants did not have a problem with collecting saliva from their child, whereas two reported it was a small problem.
VOC Badge	Watch instructional video. Remove VOC from can and attach screen guard. Wear for 48 hrs. Record dates and times. After 48 hrs, remove screen guard and separate sections of badge. Attach caps to open ends. Return to can for storage in freezer. Package sample for shipment.	12 (for assembling VOC badge)	5	One third said it was not a problem to assemble the badge and have their child wear it. One third said it was a small problem. One third said it was very difficult to assemble the VOC badges and obtain the cooperation of their child to wear it. There were problems in making the videos available to participants for viewing.
HOBO worn with VOC	Attach HOBO to shirt near VOC Badge. Wear for 48 hrs. Record dates and times. Return to plastic box for storage. Package sample for shipment.	5[3]	3	One child did not want to wear the HOBO while at camp because there were hobos nearby and was worried about being teased.
HOBO (Temp)	Remove HOBO from package and place on table or shelf. Place thermometer near HOBO. Twice per week record the date, time, and temperature for 6 weeks (42 days) on a data sheet. Package materials for shipment.	2 30[4]	2	Participants reported that it was not a problem to setup the HOBO or record the room and outdoor temperature.
MetaQx and Activity Diary	Questionnaire and activity diary are to be completed day after samples are collected using WebTV.	7	3	It was difficult to make duration of activities sum to 24 hours, potentially making Qx more cumbersome.

[1] Average duration of time to complete sample activity as reported by sample participant during debriefing; unless otherwise noted.
[2] RTI estimate of level of difficulty; Scale of 1 – 5, with 1 = easy and 5 = difficult.
[3] RTI estimate of duration
[4] RTI estimate of duration; participants may not have been taking into consideration the additional time to manually record data in the debriefing questionnaire.

The development of simpler, participant-friendly measurement devices and methods are anticipated in the future. These new technologies can be readily put to use in the NCS as they become available.

1

Introduction

Interest continues to grow in environmental health studies of children. Not only do children compared to adults have a higher physiological susceptibility to adverse exposure effects as their body systems develop, their behaviors often increase the likelihood that they will ingest or absorb various ambient environmental contaminants. To address the special risks that young children encounter as part of their daily lives, President Clinton signed the Children's Health Act of 2000 on October 17, 2000. This laid the groundwork for planning a major prospective cohort study on the impact of environmental exposures on children's health known as the National Children's Study (NCS). This report presents the results of a set of demonstration studies that were conducted as a pilot study to support the planning and implementation of the NCS.

Longitudinal cohort studies that obtain detailed exposure data on multiple chemicals for young children over time have an opportunity to identify specific exposures that may cause adverse health outcomes. Because the age at exposure and route of exposure may affect the nature and magnitude of such adverse effects, measurements from different environmental media repeated over time are necessary to thoroughly assess the impact of environmental exposures on children.

However, the burden on study participants from prolonged and obtrusive exposure measurement efforts would likely compromise a long-term study's success. For example, many participants would probably drop out of the study, and those who remain in the study might differ in important ways from those who leave. Even if participants remain in the study, their degree of compliance with complicated instructions for obtaining samples might diminish over time. Also, participants might alter their activities around obtrusive monitors (e.g., cigarette smokers may consciously or unconsciously smoke away from an air monitor). Institutional Review Boards may determine that the participant burden imposed on participating families is inappropriate for studies of children and new mothers, two population subgroups that are given special consideration by IRBs. Finally, if the complexity and cost of exposure monitoring

become excessive, financial constraints may preclude a study's implementation or completion.

These demonstration studies were designed to address some of these problems through the use of data collection methods that impose a minimal burden on the study participants while maintaining high data quality. Broad study objectives included:

- assessing the feasibility of recruiting and retaining study participants (children and their caretakers) in a set of longitudinal exposure studies,
- assessing the feasibility of employing readily available and easy to use sampling methods, instruments, and/or techniques, and
- demonstrating the feasibility of remote data collection methods with readily available, easy to use, state-of-the-art methods, instruments, and techniques for assessing human exposures to environmental contaminants.

We chose existing data collection methods that are most efficient for obtaining standard questionnaire data, activity patterns data, and measurement data on pollutant concentrations. An important feature of the study was the use of remote data collection through a Web-based panel. The approach integrates an efficient, low-burden method for identifying study subjects and collecting metadata via the web with the collection of biological and environmental samples from the same subjects. The application of these technologies was aimed at reducing the need for field investigators who have traditionally been an essential, but expensive, component of environmental field data collection. Important questions that were addressed in the study include those presented in the accompanying box.

Key Questions Addressed in the Demonstration Studies

- Can study subjects be successfully recruited through a pre-existing web-enabled panel?
- Are the incentives used in the study appropriate for level of burden?
- Is the Web a feasible way of collecting questionnaire, activity, and food diary data?
- Can study participants coordinate the temporality requirements of collecting questionnaire data shortly after biological and environmental samples have been collected?
- Can study subjects follow instructions and successfully assemble and/or use equipment for collecting samples of food and water, volatile organic compounds, urine, hair, breast milk, and others?
- Can study subjects successfully receive supplies and ship samples?

The demonstration studies were conducted under a task order contract with U.S. EPA. The scope of the task order included developing a quality systems implementation plan (QSIP); obtaining study approvals from EPA and RTI Institutional Review Boards (reported in Section 2.9); conducting focus groups meetings; and conducting the demonstration studies, which are described in this report.

2

Study Methods

2.1 Overview of Study Design

Selected Design Features of the Demonstration Studies

- An existing web-enabled panel was recruited and received information about the study via interactive television and the web.
- Study communications and questionnaire data were collected via innovative IT devices that were already in study subject's homes.
- Questionnaire data and biological and environmental samples were collected for members of each of three cohorts (0-1, 3-5, 6-8 years old) that initially consisted of 9 subjects in each.
- Environmental and biological sampling equipment were shipped to study subject's homes; study subjects collected samples. No technicians were sent into the field.
- Instructional materials were provided via the web and with shipments.
- Quality assurance included telephone and in-home visits.

Planning for the demonstration studies commenced in Summer 2001 and field data collection started in February 2002. The demonstration project consisted of three separate studies involving parents and children of three birth cohorts: 0 to 1 years old, 3 to 5 years, and 6 to 8 years. Selection of these age groups for the studies was made by U.S. EPA investigators to provide a broad distribution of children age groups and to test a range of data collection methods and study burden issues.

Study participants originated from a nationally representative Web-enabled panel developed by Knowledge Networks (KN). The Web-enabled panel, as discussed further below, is based on a probability-based random-digit dial (RDD) sample drawn from all 10-digit telephone numbers in the U.S. Panelists utilize an Internet appliance that connects to a television with Web access.

The demonstration study involved nine study participants (children-parent pairs) in each of the three birth cohorts. Study subject candidates were randomly selected from across the nation and came from homes from diverse income strata and urban and rural environments. All households recruited into the demonstration studies provided consent during enrollment and granted permission to obtain survey, physical, chemical, and biological data.

For each cohort, we collected metadata through an on-line questionnaire and biological

and environmental samples. ***Exhibits 2-1, 2-2, and 2-3*** present the sampling schema for each of the three demonstration studies. Sample collection started in February 2002 for the 0-1and 6-8 cohorts. Sampling for the 3-5 cohort started in March 2002. Sampling waves were generally staggered so that in any given week, shipping preparation activities focused on a particular type of sample for one of the cohorts. ***Exhibit 2-4*** presents the sampling schedule established at the beginning of the study.

A sampling wave started with an e-mail message sent by KN to the study participants alerting them that sample collection materials were being sent early the following week. Laboratory staff generally shipped materials on a Monday (unless it was a federal holiday). Receipt of the shipment with the sample collection materials coincided with the release of the web-based metaquestionnaire. Participants were instructed to complete the questionnaire only after (and shortly after) collecting the biological and environmental samples. Participants were asked to ship the samples back to the laboratory after they had been collected. ***Exhibit 2-5*** shows the activities conducted by the laboratory and KN that needed to be coordinated for each sampling wave. A measure of success for the demonstration studies was the extent to which study subjects completed the questionnaire after collecting the samples and the amount of time that they took to collect the samples and return them after they received the shipment. On the third and seventh day after a questionnaire was released, KN sent reminder e-mails to encourage study subjects to complete the survey if they had not done so. Telephone call reminders were placed when study subjects did not respond after one month.

Exhibit 2-1. Samples and Metaquestionnaire Content Collected for 0-1 Cohort

Biological Sample Collection	Environmental Sample Collection	Target No. of Samples per Year per Home	Metadata Question (Content)	Indicators of Compliance
Urine—one sample collected overnight on a specified day using specially prepared diapers	Breast milk[1]—one sample collected on a specified day	12 milk, 12 urine Monthly	Questions related to mother's daily activities with exposure questions related to breast-feeding and infant behaviors	Urine—presence of creatinine; evidence that sample was prepared and shipped properly Breast milk—evidence that the breast pump was used; visual inspection of sample upon receipt
	Once breast-feeding stops, 1 day duplicate food sample collected		Food diary	

[1]Breast milk sample considered to be an environmental sample (or source of exposure) with respect to the infant.

Exhibit 2-2. Samples and Metaquestionnaire Content Collected for 3-5 Cohort

Biological Sample Collection	Environmental Sample Collection	Target No. of Samples per Year per Home	Metadata Question (Content)	Indicators of Compliance
Urine—one sample collected on a specified day	Cotton socks—worn by children in the home for 1-2 hours on the day before the urine sample was collected	4 urine, 4 sets of socks Months 2, 5, 8, 11	Time and activity diary data for day of wearing the socks. Questions related to types of sources and times/activities in specific locations of exposure sources	Urine—presence of creatinine; evidence that the sample was prepared and shipped properly Socks—visual inspection of sample upon receipt
Hair—one sample collected on a specified day	Vacuum cleaner dust—collected immediately after hair collection	3 hair, 3 dust Months 3, 6, 9	Date of last change of vacuum cleaner bag; questions about vacuuming frequency, areas vacuumed and potential sources	Hair—evaluate appearance of sample; evidence that hair is bundled properly and sufficiently long Dust—visual inspection
None	Tap water—one sample collected on a specified day	3 water Months 4, 7, 9	Date and time of collection; questions about water supply system and potential sources	Tap water—compare pH measured at time of receipt to pH measured by study participant.

Exhibit 2-3. Samples and Metaquestionnaire Content Collected for 6-8 Cohort

Biological Sample Collection	Environmental Sample Collection	Target No. of Samples per Year per Home	Metadata Question (Content)	Indicators of Compliance
Saliva—one sample collected on a specified day	Settled dust collected using a surface wipe	4 dust, 4 saliva Months 1, 4, 7, 10	Dates of collection. Questions about potential sources and activities	Saliva—sodium analysis, visual inspection. Dust wipe—visual inspection
None	Personal VOC badge; (with HOBO light sensor). Collected for 2 days	2 samples Months 5, 8	Questions about potential sources and activities	Measurement of VOC's in samples received; visual inspection; evaluation of light sensor data
None	Electronic temperature/relative humidity (HOBO) logging data for 2 months with periodic manual recordings of temperature	2 samples Months 6, 9	Dates, times; window open/closed; values observed; concurrent outdoor temperature and source of information, whether rained in past 24 hours	Comparison of the temperature logged by the device with those recorded by study participants

Exhibit 2-4. Longitudinal Collection of Metaquestionnaire Data and Samples by Cohort and Month

		2002												2003
Age	**Measurement Parameter**	**Feb** 19 2	**Mar** 18	**Apr** 2 15 2	**May** 13 20 2	**Jun** 10 17 24	**Jul** 8 15 22	**Aug** 5 12 19	**Sep** 3 9 16 30	**Oct** 7 14 28	**Nov** 4 11 25	**Dec** 9 2	**Jan** 6 20
0 to 1	Urine (U)	U		U U	U	U	U	U	U	U	U	U	U
	Breast Milk or Diet (M)	M		M M	M	M	M	M	M	M	M	M	M
	Questionnaire (Q)	Q		Q Q	Q	Q	Q	Q	Q	Q	Q	Q	Q
3 to 5	Urine (U)		U			U			U		U		
	Cotton Socks (S)		S			S			S		S		
	Questionnaire (Q)		Q			Q			Q		Q		
	Hair (H)			H			H		H				
	Vacuum Dust (V)			V			V		V				
	Questionnaire (Q)			Q			Q		Q				
	Tap Water (W)				W			W		W			
	Questionnaire (Q)				Q			Q		Q			
6 to 8	Saliva (S)	S			S			S			S		
	Dust Wipe (D)	D			D			D			D		
	Questionnaire (Q)	Q			Q			Q			Q		
	VOC Badge (V)					V			V				
	Questionnaire (Q)					Q			Q				
	HOBO (H)						H			H			
	Questionnaire (Q)						Q			Q			

Exhibit 2-5. Target Days for Sampling and Web Data Collection for a Sampling Event

Day	Web Data Collection	Sample Collection
Friday	E-mail sent from KN alerting participants that sampling materials are being shipped next week.	
Monday		Sampling materials shipped by laboratory staff
Tuesday	Metaquestionnaire made available to participants via web.	Sampling materials received by participant
Wednesday	Metaquestionnaire completed and received by KN[1]	Sample collected by participant[1]
Thursday		Sample and sampling equipment shipped by participant to laboratory[1]
Friday	Metaquestionnaire reviewed for completeness[1]	Sample examined for proper collection, storage and shipment[1]

[1]Target days for completion of activity

2.2 Web-enabled Data Collection and Panel Description

An important objective of the demonstration study was to assess the feasibility of using remote data collection methods. Web data collection is one approach that may be appropriate for collecting some data for the NCS. The existing panel assembled by Knowledge Networks provided an opportunity to evaluate this approach for exposure monitoring.

2.2.1 Sampling Methodology for the Web-enabled Panel

Knowledge Network's Web-enabled panel is based on a nationally representative, list-assisted, random-digit-dial (RDD) sample drawn from all 10-digit telephone numbers in the United States. Only those banks of telephone numbers that have zero directory-listed telephone numbers are *excluded*. Telephone numbers are selected from the 1+ banks with equal probability of selection for each telephone number. Telephone exchanges with concentrations of Hispanics and African-Americans are oversampled. Sampling is implemented without replacement to ensure that telephone numbers already fielded are not fielded twice.

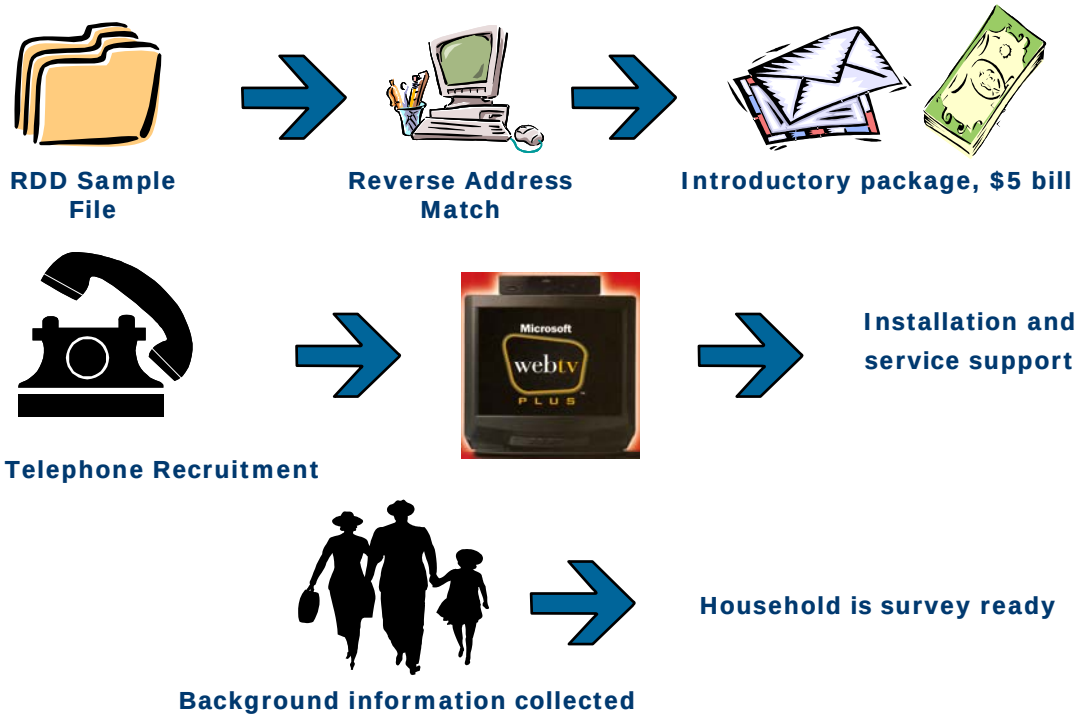
The sample is first screened for confirmed disconnected telephone numbers and for businesses. Next, the sample is screened to exclude telephone numbers that are not in the WebTV Internet Service Provider network. This process results in the exclusion of approximately 6 percent to 8 percent of the U.S. population. Additionally, households that do not have a telephone are not covered in the sample (approximately 6 percent of the U.S.

households).

2.2.2 Recruitment Procedures for the Web-enabled Panel

Exhibit 2-6 illustrates the KN panel recruitment procedures. All telephone numbers that pass the screening process are sent to a commercial reverse address-matching service. All telephone numbers matched to an address receive an advance letter and $5 cash incentive. A random 50 percent subsample of the unmatched telephone numbers is also included in the final sample of telephone numbers sent for recruitment. All telephone numbers passing the screening process are sent to a telephone interviewing organization for recruitment. Cases are dialed up to 90 days, with at least 15 dial attempts on cases in which no one answers the telephone and 25 dial attempts on telephone numbers known to be associated with households. Extensive refusal conversion is also performed.

Exhibit 2-6. Web-enabled Panel Recruitment Procedures



Experienced interviewers conduct all recruitment interviews. During the 10-minute interview, interviewers ask to speak with an adult household member who is told that they have been selected to join the research panel. Respondents are instructed that in exchange for

participation in short weekly surveys over a 2- to 3-year period, the household is provided with free hardware (an Internet appliance that connects to a television), free Internet access, free password-protected e-mail accounts for each household member age 13 and older, ongoing technical support, and an incentive program to encourage continued participation. All members in the household are enumerated, and some initial demographic variables and background information on prior computer and Internet usage are collected.

To ensure consistent delivery of survey content, each household is provided with identical hardware, even if they currently own a computer or have Internet access. Microsoft's WebTV is the hardware platform currently used. The device consists of a set-top box that connects to a TV and the telephone. It also includes a remote keyboard and pointing device. The WebTV device has a built-in 56K modem that provides the household with a connection to the Internet. The base unit also has a small hard drive to accommodate large file downloads, including video files. File downloads do not require any user intervention and usually occur at night.

Prior to shipment, each unit is custom configured with individual e-mail accounts so that it is ready for immediate use by the household. Most households are able to install the hardware without additional assistance. Knowledge Networks maintains a telephone technical support line and will, when needed, provide on-site installation. The call center also contacts household members who do not respond to e-mail and attempts to restore contact and cooperation.

All new panel members are sent an initial survey (i.e., the Adult Profile Survey) to confirm equipment installation and familiarize them with the WebTV unit. Demographics such as gender, age, race, income, and education are collected for each participant to create a member profile. This information can be used to determine eligibility for specific studies and does not need to be gathered with each survey.

2.2.3 Survey Administration Procedures for the Web-enabled Panel

To initiate a survey, an e-mail message is sent to the panel members selected for the survey. The e-mail invitation includes the key elements of an advance letter and informs the recipient that a survey is waiting for him/her. The participant clicks on a button within the e-mail to start the multimedia questionnaire. In general, nonrespondents to surveys are sent up to two e-mail reminders to complete the survey. Telephone prompting to complete the survey via

the Internet may also be employed. The Internet-connected family television set, rather than a computer screen, serves as the monitor on which surveys are viewed and completed. All Web-enabled panel surveys are self-administered, which allows respondents to complete the surveys at their convenience in the comfort and privacy of home. Survey consistency across households is assured because each household receives the same standardized hardware and high-speed network connectivity. Therefore, each panel member receives the same stimulus. By controlling the platform used by respondents, consistency in survey administration is achieved. From the respondent's point of view, the inclusion of video, audio, and 3-D graphics in the questionnaire makes the survey experience much more engaging and less burdensome than conventional telephone interviews.

The survey administration procedures specific to the demonstration studies are described under Study Methods, Sections 2.4, 2.5, 2.6.

2.3 Selection and Recruitment of Study Subjects

2.3.1 Sample Selection of Study Subjects

We selected parent-child study participant pairs from Knowledge Networks' nationally representative web-enabled panel of U.S. households. We used pre-existing household data to identify groups of households that have children in each of the three age cohorts: 0-1, 3-5, and 6-8 years of age. For each group, we then used the adult panel members' household information as the basis for forming three sampling domains shown in ***Exhibit 2-7***. Using these three domains, we developed nine household strata per cohort by crossing the three categories of income by region, and by rural area. The nine strata per cohort are reflected in ***Exhibit 2-8*** below.

We imposed the requirement that participants with children in the 0-1 age cohort must be breast feeding. To operationalize this requirement, we used household data to identify pregnant women in their third trimester and/or women who had just given birth. We administered a brief screener questionnaire over the Web via interactive TV to ascertain if the pregnant women, or other women who had just given birth, were planning to breast feed. We recruited with certainty any women who recently gave birth during the past three months, were already breast feeding and planned to do so for at least three months. Additionally, we also sampled with certainty

pregnant women who were giving birth within six weeks of the screener and planned to breast feed. Because many households contained age-eligible children, we further imposed the condition that a household may only be included in one cohort study. If a household fell into more than one age eligible cohort, we randomly selected which cohort for inclusion.

Exhibit 2-7. Sampling Domains for Sample Selection

Domain	Definition
Household income	
Low	Less than $24,999
Medium	Between $25,000 and $59,999
High	More than $60,000
Urbanicity	
Urban/Suburban	Metropolitan areas
Rural	Non-metropolitan areas
*Region**	
East	New England, Middle Atlantic, South Atlantic, East North Central, and East South Central
West	Pacific, Mountain, West North Central, and West South Central

**U.S. Census categories*

Exhibit 2-8. Nine Strata Per Cohort

Strata
Low Income ─ Rural
Low Income ─ East/Urban
Low Income ─ West/Urban
Medium Income ─ Rural
Medium Income ─ East/Urban
Medium Income ─ West/Urban
High Income ─ Rural
High Income ─ East/Urban
High Income ─ West/Urban

2.3.2 Recruitment of Study Subjects

We randomly ordered the households that met the sampling and eligibility criteria into nine separate strata lists per cohort. Our initial approach was to recruit one household per list by choosing the first household on the list, and contacting them through an e-mail message sent over the Web via interactive TV. The recruitment e-mail ***(see Appendix A)*** described the purpose, sponsor, and requirements of the study. It asked the panel member if he or she was willing to participate in the demonstration study. As part of this e-mail survey, we also collected the age of the child in order to confirm the information we already had on the household and ensure it contained age appropriate children. Once a household agreed to participate in the study, we mailed the informed consent form (See Section 2.9 and ***Appendix B)*** along with a cover letter that summarized the requirements outlined in the e-mail. Households that did not return the informed consent within one week were prompted by telephone.

When a household refused to participate, we contacted the subsequent household on the list and re-initiated the process described above. However, about one month into participant recruitment, we altered our approach to contact multiple households per cohort in parallel. The elapsed time for the overall recruitment process during the busy holiday season (i.e., recruitment e-mail, mailing of the informed consent, telephone follow-up, and receipt of the consent form) was longer than anticipated. To meet the study schedule, we revised the recruitment e-mail to indicate that the household *may* be selected to participate, and that we would re-contact them at the end of the recruitment period. Once all nine cells across all cohorts were filled with at least one or more eligible households, we selected one household per strata per cohort to participate in the demonstration studies. We sent a confirmation/welcome e-mail to those households that were selected to participate and a thank you e-mail to the households that were not selected.

2.4 Study Methods: 0-1 Cohort – Breast Milk, Food, Beverage and Urine

In this cohort, emphasis was placed on the collection of breast milk, beverage, or food that the baby consumed (environmental) and on urine from the baby (biological).

2.4.1 Questionnaires, Diaries, and Instructional Materials

The metaquestionnaire used for this cohort was designed to obtain information that might be linked to exposures to metals. Metals could be absorbed by the mother following exposures

via dust, vapors, industrial emissions, work with metals, herbal supplements, and foods, especially seafood (mercury, arsenic). Although kept purposefully short, the questionnaires asked about possible exposures derived from activities, proximity to industry, and ingestion exposures. A question was also included to probe an aspect of the child's development that could be affected if exposures to metals were occurring. The metaquestionnaire for this cohort can be found in ***Appendix C-1.***

The diary for this cohort was a food diary developed to obtain information about the types and quantities of foods/beverages consumed by the infant. Data were input as described in Section 2.7 to capture each food item at each meal. The diary also sought to understand how the food was handled so that any contamination by dust, from either surfaces or transfer to the food via hands, might have contributed to ingestion exposure.

Instructional materials were prepared and accompanied each shipment. These multiple-page instructions described and showed participants what was contained in the shipment, how it was to be used, and how it was to be shipped back. A one-page version of the instructions was also provided to the participants to serve as a quick reference guide. Instructions were also available via the Web. A checklist was also provided to help participants remember to include all of the items originally sent to them in the return shipment. Copies of instructional materials are shown in ***Appendices D-1, E-1, and F-1***.

A debriefing questionnaire was developed for the 0-1 cohort that was administered at the end of the study ***(Appendix G-1)***. This study instrument requested information about the study subject's impressions of the sampling equipment and procedures, ease of completing the metaquestionnaire, and appropriateness of the incentives.

2.4.2 Biological and Environmental Sample Collection

Prior to use, all sample collection materials (breast pump, collection bottles, etc.) were verified to be clean with regard to the potential target metals. The collection bottles were soaked in concentrated nitric acid at least overnight. They were rinsed with de-ionized water before being tested using the following procedure. The breast pump/sample bottles were rinsed/equilibrated with dilute acid. The recovered leachate was analyzed by ICP/MS to determine the elements present. The extracts were shown not to contain metals that would contaminate the sample during collection and storage. Sample collection materials were

prepared and packaged as described in ***Appendix H-1*** and shipped to the participant along with a pre-paid FedEx return-shipping label as described in ***Appendix D-1***. The breast pump was considered to be a personal item; the same pump was used for each participant each time. It was returned to RTI for cleaning in order to be sure that all pumps were subject to the same cleaning procedure.

2.4.3 Compliance Monitoring and Sample Analysis

When samples were received at RTI from participants, they were inspected and logged into an Access database with a Visual Basic interface. This interface prompted the person logging in samples to answer a series of questions that would later be used to assess compliance and the condition of samples upon receipt. The questions used for the 0-1 cohort are shown in ***Appendix I-1.***

As a further measure of compliance for urine collection, samples collected in Months 1, 6, and 8 (February, July, and September) were analyzed for creatinine. The pads containing the desired urine samples were thawed, and the urine was expressed into a urine container provided by Quest Diagnostics, the vendor that conducted the creatinine analyses. Samples were analyzed for creatinine using a spectrophotometric assay as described in the QSIP for this project. A total of four blanks (deioninzed water) were sent for analysis to serve as laboratory blanks.

The timeliness with which samples were returned was also evaluated. A target of sample collection within seven days of participant receipt of sample collection materials was established for all sample types in this cohort. We considered the *last* day of sample collection to be the collection date for all samples collected in the demonstration studies.

2.5 Study Methods: 3-5 Cohort – Urine/Socks, Hair/Vacuum Dust, Tap Water

In this cohort, three different types of samples were used. The first set of samples consisted of socks worn by the child to collect dust and this was linked to urine. Such a pairing would be amenable to the study of metals or pesticides, depending on how the samples were analyzed. The second set of samples combined vacuum dust and hair, a scenario that could be used to evaluate chronic exposures to metals in the environment. Finally, tap water was collected. These combinations were chosen to cover a range of sample types that would potentially be utilized in a longitudinal study.

2.5.1 Urine and Socks

In this set of samples, pre-cleaned, white cotton socks were provided and were to be worn, without shoes, by the child for a 2-hour period while indoors. A urine sample was requested for the next morning. This mimics a link between dermal exposure to pesticides via floor dust with pesticides/metabolites measured in urine the following day. This sample type was collected quarterly over the course of the year.

Questionnaires, Diaries, and Instructional Materials. The metaquestionnaire used for this group focused on pesticide use in and around the home as well as at any daycare centers that the child might attend. In each case, information on the pesticides used, the form in which they were applied or used, and the places of application were gathered. This included both indoor and outdoor uses as well as the types of pests for which the pesticide was applied. In addition, questions were asked about the types of foods the child ate within the last 24 hours, whether or not the child's hands were washed before meals, and fractions of time the child spent in various microenvironments both inside and outside of the home. The metaquestionnaire for this set of samples, including the activity diary for the socks, can be found in ***Appendix C-2***.

Instructional materials were prepared and accompanied each shipment. These instructions described and showed participants what was contained in the shipment, how it was to be used, and how it was to be shipped back. A one-page version of the instructions was also provided to the participants to serve as a quick reference guide. Instructions could also be viewed via the Web in the event that hardcopy instructions were misplaced. A checklist was provided to help participants remember to include all of the items originally sent to them in the return shipment. These instructions are shown in ***Appendices D-2, E-2, and F-2***.

A debriefing questionnaire was developed for the 3-5 cohort that was administered at the end of the study ***(Appendix G-2)***. This questionnaire requested information about the study subject's impressions of the sampling equipment and procedures for the urine and socks (and other sampling procedures for the 3-5 cohort).

Sample Collection. Prior to use, all sample collection materials (socks, collection bottles, etc.) were cleaned. Sample collection materials were prepared and packaged as described in ***Appendix H-2*** and shipped to the participant along with a pre-paid FedEx return-shipping label as described in ***Appendix D-2***.

Compliance Monitoring and Sample Analysis. When samples were received at RTI from participants, they were inspected and logged into an Access database with a Visual Basic interface. This interface prompted the person logging in samples to answer a series of questions that would later be used to assess compliance and the condition of samples upon receipt. The questions used for the 3-5 cohort are shown in ***Appendix I-2***.

As a further measure of compliance for urine collection, samples collected in Months 2, 8, and 11 (March, September, and December) were analyzed to determine if creatinine was present. The measurement of creatinine indicates the presence of urine. Urine samples in the specimen cups were allowed to thaw and an aliquot was transferred into a urine container provided by Quest Diagnostics. Samples were analyzed using a spectrophotometric assay. A total of four samples were sent for analysis to serve as laboratory blanks. In addition, aliquots of two of the urine samples were split and sent for analysis in two different batches. A comparison of the measured creatinine values in these split samples served as an indicator of inter-day precision.

The timeliness with which samples were returned was also evaluated. A target of sample collection within seven days of participant receipt of sample collection materials was established for this set of samples.

2.5.2 Hair and Vacuum Dust

In this subset of samples, a sample of hair was collected along with vacuum dust from the home vacuum cleaner. This environmental/biological sample pair was chosen to mimic the evaluation of the longer-term exposure to metals via dust to their accumulation in hair. Questions about hair and vacuum dust collection were included on the debriefing questionnaire.

Questionnaires and Instructional Materials. To minimize the burden to the participant, the metaquestionnaire ***(Appendix C-2)*** asked many of the same questions as the sock/urine survey. Although this sample pair was more appropriate to metals, this demonstration study was not designed to be a full-scale exposure study but rather a test of the ability of participants to handle questionnaires and various sample collection approaches. An additional question was added that defined whether or not the child's hair had been washed that day. That

would be important to know in order to differentiate between metals or other compounds in the hair vs. on the hair.

Instructional materials were prepared and accompanied each shipment. These instructions described and showed participants what was contained in the shipment, how it was to be used, and how it was to be shipped back. A one-page version of the instructions was also provided to the participants to serve as a quick reference guide. A checklist was provided to help participants remember to include all of the items originally sent to them in the return shipment. These instructions are shown in ***Appendices D-2, E-2, and F-2***. It is important to point out that this mode of dust collection assumed that participants used vacuum cleaning systems in which dust was collected in the dry state. One of the participants owned and used a Rainbow vacuum cleaner that collects dust into water. This problem was discussed and the participant was instructed to collect dust by disassembling the vacuum cleaner and scraping dust out of the tubing that leads to the water. The collected dust was placed into a small, zip-loc bag.

Given the possible difficulty in conveying to the participant the appropriate method to collect the hair sample, a short (approximately 1 minute) video was prepared. This video was available via the Web for participants to view. It was thought this might provide for the most consistent sample collections. In addition, demonstration of the use of video instructions and an evaluation of participant's use of such a medium would help to define how future studies could convey visual information. A copy of the video is supplied separately with this report and the script can be found in ***Appendix D-2***.

Sample Collection. Prior to use, all sample collection materials (scissors, comb) were cleaned. Sample collection materials were packaged as described in ***Appendix H-2*** and shipped to the participant along with a pre-paid FedEx return-shipping label as described in ***Appendix D-2***.

Compliance Monitoring and Sample Analysis. When samples were received at RTI from participants, they were inspected and logged into an Access database with a Visual Basic interface. This interface prompted the person logging in samples to answer a series of questions that would be used later to assess compliance and the condition of samples upon receipt. The questions used for the 3-5 cohort are shown in ***Appendix I-2***.

The timeliness with which samples were returned was also evaluated. A target of sample

collection within seven days of participant receipt of sample collection materials was established for this set of samples.

2.5.3 Tap Water

In this subset of samples, tap water was the focus of collection efforts. There was no biological sample collected concurrently with the collection of tap water. Tap water collected in this study could be used to evaluate drinking water as a source of exposures to pesticides, metals, and other toxic compounds. (An increased use of bottled water for drinking purposes can affect the impact of tap water on total exposures, but studies can be designed to take this into account.) No preservative, such as sodium thiosulfate, was added to the water at the time of collection. It was never anticipated that these samples would be analyzed. A preservative would be necessary to prevent further action of water disinfectants (residual chlorine, chloramines) on chemicals in the water during transport.

Questionnaires and Instructional Materials. The questions asked of this cohort (Section 2.7) consisted of items related to the source of their dinking water, whether or not they used water treatment, what water the child drank, how long the water was run before a glass for drinking was taken for consumption, what other beverages were mixed using the tap water, and how much tap water was directly consumed by the child. The questionnaire for this set of samples can be found in ***Appendix C-2***. Questions about tap water collection were included on the debriefing questionnaire.

Instructional materials were prepared and accompanied each shipment (see below). These instructions described and showed participants what was contained in the shipment, how it was to be used, and how it was to be shipped back. A one-page version of the instructions was also provided to the participants to serve as a quick reference guide. Instructions were also available via the Web. A checklist was also provided to help participants remember to include all of the items originally sent to them in the return shipment. These instructions are shown in ***Appendices D-3, E-3, and F-3***.

Sample Collection. Sample collection materials were prepared and shipped as described in ***Appendix H-2***.

Compliance Monitoring and Sample Analysis. When samples were received at RTI from participants, they were inspected and logged into an Access database with a Visual Basic interface. This interface prompted the person logging in samples to answer a series of questions that would later be used to assess compliance and the condition of samples upon receipt. The questions used for the 3-5 cohort are shown in ***Appendix I-2***.

The timeliness with which samples were returned was also evaluated. A target of sample collection within seven days of participant receipt of sample collection materials was established for this sample type.

2.6 Study Methods: 6-8 Cohort – Saliva/Dust, VOC/HOBO (Light Intensity), HOBO (Temperature/Relative Humidity)

In this cohort, three different types of samples were used. The first set of samples, collected quarterly, consisted of saliva and settled dust collected using a dust wipe. The second set of samples was badges designed to collect volatile organic compounds (VOCs) over a 48-hour period (2 sampling periods). VOC collection was linked with measurement of light intensity via HOBO. Connecting light intensity measurements with the VOC badge provided an indication of whether the badge had been worn. Finally, a small monitor (HOBO) was deployed that would track temperature and relative humidity for 42 days.

2.6.1 Saliva and Dust Wipe

Questionnaires and Instructional Materials. The metaquestionnaire developed for this set of samples ***(Appendix C-3)*** focused on whether or not there were smokers in the home, use of materials that would release VOCs, whether or not windows were open/closed, and riding in motor vehicles. In addition, there were questions that asked about time spent in various microenvironments.

Instructional materials were also sent to participants with each shipment. These instructions described and showed participants what was contained in the shipment, how it was to be used, and how it was to be shipped back. A one-page version of the instructions was also provided to the participants to serve as a quick reference guide. Instructions were also available over the Web in case the hardcopy version was misplaced. A checklist was also provided to help participants remember to include in the return shipment all of the items originally sent to them. These instructions are shown in ***Appendices D-3, E-3, and F-3***.

A debriefing questionnaire was developed for the 6-8 cohort that was administered at the end of the study ***(Appendix G-3)***. This questionnaire requested information about the study subject's impressions of the sampling equipment and procedures for the saliva and dust wipes (and other sampling procedures for the 6-8 cohort).

Sample Collection. Sample collection materials were prepared and packaged as described in ***Appendix H-3*** and shipped to the participant along with a pre-paid FedEx return-shipping label as described in ***Appendix D-3***.

Compliance Monitoring and Sample Analysis. When samples were received at RTI from participants, they were inspected and logged into an Access database with a Visual Basic interface. This interface prompted the person logging in samples to answer a series of questions that would later be used to assess compliance and the condition of the samples. These questions are shown in ***Appendix I-3***.

The timeliness with which samples were returned was also evaluated. A target of sample collection within seven days of participant receipt of sample collection materials was established for this set of samples.

2.6.2 VOC Badge and HOBO/Light Intensity

In this subset of samples, a 3M 3520 Organic Vapor Monitor badge was used in conjunction with a continuous light monitor/data logger (HOBO). Exposures to VOCs are common and the 3M badge is a convenient way to obtain a time-weighted average of exposure to volatile chemicals. The VOC badge is a passive device approximately 43 mm in diameter and 23 cm thick worn by participants by attaching the clip to their clothing. Prior to use, it must be removed from the sealed can and assembled properly (see instructional materials section below). Use of this device is complicated and its use was designed to see if participants could successfully collect a sample. The HOBO (Anset Computer Corporation) is a small monitoring device (58 x 44 x 17 mm) that is capable of recording relative humidity, temperature, and light intensity. It can be pre-programmed to start and stop data logging prior to shipment. Data from the logger are downloaded and the device is programmed through the use of a PC and manufacturer-supplied software. For this application, the HOBO was pre-programmed to stop

light intensity data acquisition (see compliance monitoring below) after 16 days, long past the time that the VOC badge sampling should have been completed (7 days); the participant did not need to do anything with the HOBO, except to wear it along with the VOC badge during the monitoring period. No biological samples were collected in conjunction with VOC sampling.

Questionnaires and Instructional Materials. The metaquestionnaire used for this group ***(Appendix C-3)*** was the same as for the saliva/dust collection and focused on whether or not there were smokers in the home, use of materials that would release VOCs, whether or not windows were open/closed, and riding in motor vehicles. In addition, there were questions that asked about time spent in various microenvironments. Questions about VOC badge/HOBO sample collection were included on the debriefing questionnaire.

Instructional materials were prepared and accompanied each shipment. These instructions described and showed participants what was contained in the shipment, how it was to be used, and how it was to be shipped back. A one-page version of the instructions was provided to the participants to serve as a quick reference guide. Instructions were also available via the Web. A checklist was provided to help participants remember to include all of the items originally sent to them in the return shipment. These instructions are shown in ***Appendices D-3, E-3, and F-3***.

Given the possible difficulty in conveying to the participant exactly the right way to collect the VOC sample, a short (approximately 1 minute) video was prepared. This video was available via the Web for participants to view. It was thought this might provide for the most consistent sample collections. Proper assembly, use, termination of sampling and preparation for shipment of the badges was the most difficult thing asked of any of the participants. Demonstration of the use of video instructions along with an evaluation of participant's use of such a medium would help to define how future studies could convey visual information. A copy of the video is supplied separately with this report and the script can be found in ***Appendix D-3***.

Sample Collection. Sample collection materials were prepared and packaged as described in ***Appendix H-3*** and shipped to the participant along with a pre-paid FedEx return-

shipping label as described in ***Appendix D-3***. The HOBO was pre-programmed to begin and end sample collection automatically.

Compliance Monitoring and Sample Analysis. When samples were received at RTI from participants, they were inspected and logged into an Access database with a Visual Basic interface. This interface prompted the person logging in samples to answer a series of questions that would later be used to assess compliance and the condition of samples upon receipt. The questions used for the 6-8 cohort are shown in ***Appendix I-3***. Also, data from the HOBOs were downloaded and examined to determine if it appeared that the VOC badge and HOBO had been worn for 48 hours. It was assumed that major light variations would be monitored during the course of the sampling period. Relatively "flat" light signals would be anticipated only during periods when participants' were asleep or if the device was placed on a shelf and not worn.

An additional test of compliance was to actually extract and analyze the badges for VOCs to determine if the badge was really used along with the HOBO (VOCs measured) or if it was assembled properly (reasonable concentrations of VOCs measured). If unusually high concentrations were measured, one potential cause would be that the white, permeation barrier was not on the device for extended periods of time (i.e., not assembled properly or allowed to sit open during preparation for return shipment). Another possibility is that the badge fell open during return shipment and became contaminated. It was anticipated that the nine badges from the first collection would be analyzed. However, participants had trouble with this method and it was necessary to combine both sets in order to obtain nine samples that appeared to be acceptable for VOC analysis.

The first stage of each badge was extracted with carbon-disulfide/acetone and analyzed for typical indoor air VOCs by gas chromatography/mass spectrometry as described in the QSIP. Two laboratory blanks (unexposed badges) were extracted and analyzed as a measure of background. Two method controls were prepared by exposing each badge for a known time to a stream of VOC-containing nitrogen generated using a permeation system. In addition, one extract was analyzed in duplicate to assess instrumental analysis precision. Although not ideal, badges used for the blank and control samples were not taken from the same lot as those shipped to the field.

The timeliness with which samples were returned was also evaluated. A target of sample collection within seven days of participant receipt of sample collection materials was established for this sample type.

2.6.3 HOBO (Temperature)

In this subset of samples, temperature and relative humidity were the focus. There was no biological sample collected concurrently. This sample was used to determine how well an electronic device could be deployed in the home for extended periods. This was used as a model of various real-time monitors that might be anticipated to be used in future, longitudinal studies. The HOBO, however, is a very rugged device and might not be typical of all real-time monitors that might be proposed in the NCS. For this study, the HOBOs were pre-programmed to collect data for 44 days for the first shipment (July). Given that some participants delayed starting sample collection, the recording duration for the second (October shipment) was extended to 110 days.

Questionnaires and Instructional Materials. The metaquestionnaire used for this group (***Appendix C-3***) was the same as for the saliva/dust and the VOC/HOBO collections and focused on whether or not there were smokers in the home, use of materials that would release VOCs, whether or not windows were open/closed, and riding in motor vehicles. In addition, there were questions that asked about time spent in various microenvironments. Questions about HOBO (temperature) data collection were included on the debriefing questionnaire.

Instructional materials were prepared and accompanied each shipment (see below). These instructions described and showed participants what was contained in the shipment, how it was to be used, and how it was to be shipped back. A one-page version of the instructions was also provided to the participants to serve as a quick reference guide. Instructions were also available via the Web. A checklist was also provided to help participants remember to include all of the items originally sent to them in the return shipment. These instructions are shown in ***Appendices D-3, E-3 and F-3***.

Sample Collection. Materials were prepared and shipped as described in ***Appendix H-3***. Following deployment in the home, participants were asked to record the temperature read

from a thermometer that was to be placed next to the HOBO for the duration of the monitoring period. The HOBO was pre-programmed to start the day after shipment and was to record data within 44 or 110 days, a period of time sufficient to cover the desired 42-day monitoring period.

Compliance Monitoring and Sample Analysis. When samples were received at RTI from participants, they were inspected and logged into an Access database with a Visual Basic interface. This interface prompted the person logging in samples to answer a series of questions that would later be used to assess compliance and the condition of samples upon receipt. The questions used for the 6-8 cohort are shown in ***Appendix I-3***. Also, data from the HOBOs were downloaded and examined to determine if it appeared that the device had not been moved around during the monitoring period.

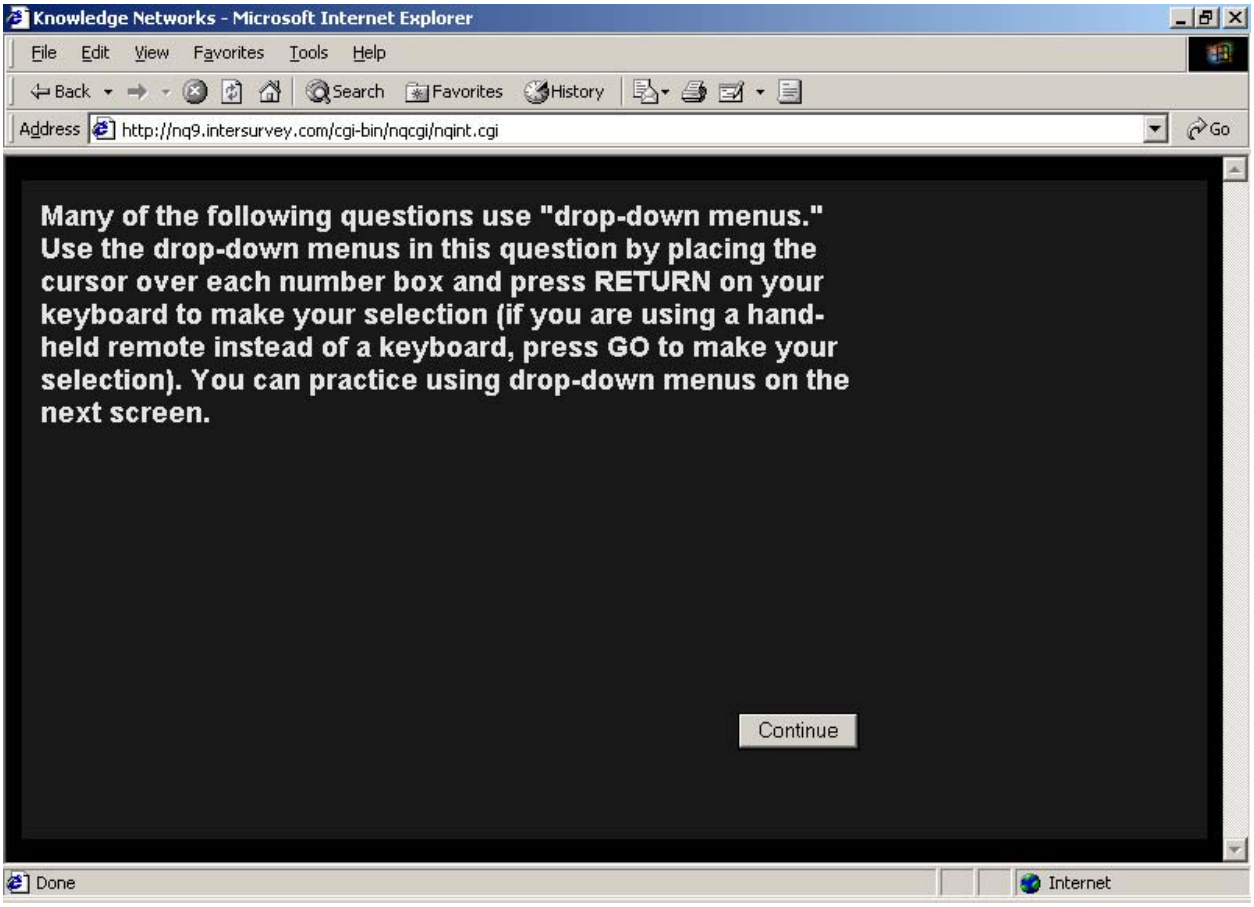
The timeliness with which samples were returned was also evaluated. A target of completion of sample collection within 49 days of participant receipt of the HOBO was established for temperature measurement in this cohort.

2.7 Web Implementation of Questionnaires and Other Materials

The metaquestionnaires, food diary, and socks activity diary (***Appendix C***) were programmed for self-administration over the web via interactive TV. While the substantive content of each questionnaire differed, each survey contained similar questions and web screen layout. Screens were designed using web survey features such as drop down menus for diaries, radio buttons for checking all that apply, and the use of still images and graphics. Several screens in each web questionnaire collected dates for the various biological or environmental specimen collections. We programmed soft checks for each date and soft checks between dates such that various prompts would appear if the subject did not record an answer, or recorded an inconsistent answer. For example, "Please provide answer" would appear if the study participant attempted to skip over date information. For inconsistent dates, the prompt, "There is a problem with the date entered. Please re-enter date" would appear.

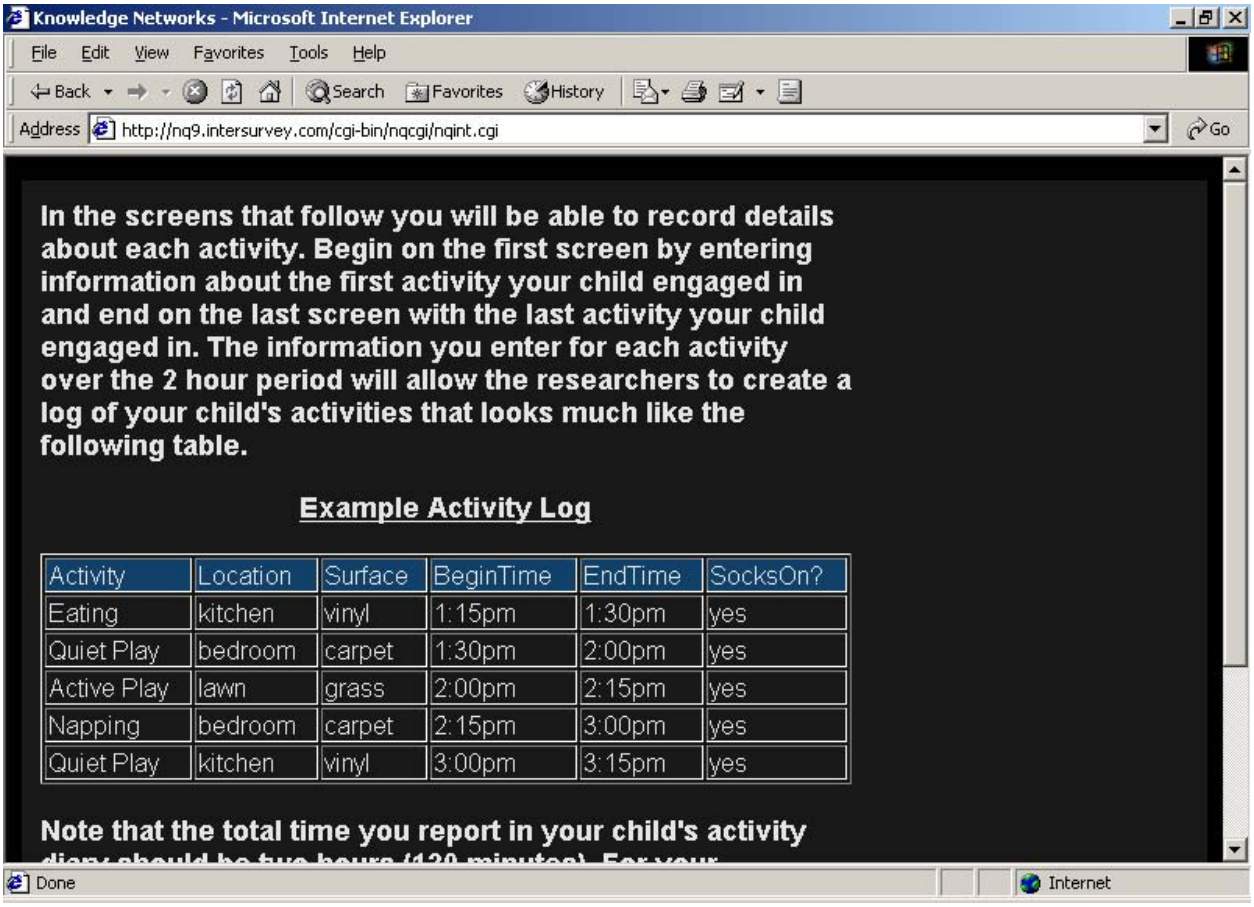
Because these surveys were self-administered, we also programmed some practice questions and provided an example of what a completed activity diary should look like. See ***Exhibits 2-9 and 2-10*** below.

Exhibit 2-9. Example Practice Drop Down Menu



As described in Section 2.5, participants learned how to properly collect and ship the biological and environmental samples in three ways, two of which exploited the benefits of web technology. Subjects were able to access a copy of the printed instructions included with each sample kit over the web on Knowledge Networks website. Instructions on accessing the online instructions were included with the prenotification e-mail that subjects received two days prior to the sample kit arriving at their homes. Another mechanism for providing instructions over the web was through the use of short video clips on how to collect the more complicated samples of hair and VOC badge. These 60─75 second videos were developed by RTI and made available to subjects via interactive TV one week prior to the sample collection. Due to technological difficulties solely related to the Web TV platform and corresponding modem speed, anywhere between 40 ─ 75% of the videos were successfully watched prior to sample collection. Future studies using video clips over the web are likely to avoid these specific difficulties with faster modem connections and a different Internet platform.

Exhibit 2-10. Example Activity Diary



2.8 Usability Testing

Prior to the start of data collection, we conducted usability testing on each of the five programmed web questionnaires and diaries, and the instructional materials that accompanied each specimen kit. Five participants (one in the 0-1 cohort, three in the 3-5 cohort, and one in the 6-8 cohort) were selected from a convenience sample of non-technical RTI staff with children in the corresponding age groups. The usability testing was conducted at RTI's usability lab and used the interactive TV platform.

For each session, the participant was asked to review the sample specimen kit, related equipment and read the instructional materials. The survey methodologist probed for areas of ambiguity or confusion. She also encouraged the participant to volunteer any feedback on how to improve the overall clarity, presentation and understanding of the instructional materials. Some of the results included the identification of minor inconsistencies between labeling of the kits and instructions, lack of clarity on using Federal Express for return shipment, and some

confusion over the packing materials. Findings from this aspect of the usability testing were incorporated and used to refine the instructional materials, contents and packaging of the specimen kits.

Following testing of the specimen kits, each participant was asked to self-administer the questionnaire, thinking aloud while they completed the interview. They were encouraged to volunteer any criticisms of the instrument and to explain any confusion they had while answering questions. During the interview, the survey methodologist made note of any data entry errors the participant made and any problems they tried to fix. For example, the interactive TV questionnaires require a respondent to press a "Submit" button after entering their answer. The first question in each questionnaire asked the respondent about their relationship to the child in question, and listed about 10 possible relationships. The "Submit" button was displayed below this list, and since the list was quite long, it was not visible on screen. Without fail, each time a participant was answering his or her first questionnaire, the participant would select the answer then wait to be taken to the next screen. After a few seconds, participants would either ask what to do next, or start pressing buttons to try to get to another question. The survey methodologist made note of this each time. The interviews continued in this manner. After completing a questionnaire, the survey methodologist administered several debriefing questions to obtain the participant's overall impression of the questionnaire.

Where possible, refinements were made to each web questionnaire and/or diary. For example, one participant was asked to record the number of hours her child spent in specific rooms within the homes. She was given a list of rooms in this order: Living Room→Dining Room→Family Room→Bedroom→Study/Library→Bathroom→Kitchen→Other**.** However, during the testing it became obvious that the participant wanted to enter the answers in order of the rooms her child spent the most hours in. She started with the bedroom, then bathroom, dining room, and living room. Since the rooms categories were not listed in this order, she arrowed up and down the list repeatedly to enter each new answer. As a result of this observation, the listed order was changed to: Bedroom→Bathroom→Kitchen→Dining room→Living room→Family room→Study/library→Other.

2.9 Protection of Study Subjects

Protection of the study subjects throughout the duration of the demonstration studies was a high priority. The IRB approval process commenced with the development of the study protocol ***(Appendix J)*** in June 2001. The protocol served as a basis for obtaining approvals from RTI and U.S. EPA. Questionnaires for all three birth cohorts were developed and submitted with the RTI and EPA IRB review package. The package was submitted to the RTI and EPA IRBs in August and October, respectively. Approvals were received from both RTI and EPA in September and November, respectively. The RTI IRB requested several changes in the consent forms, none of which changed the objectives or direction of the three demonstrations studies.

Several changes and additions to questionnaires and instructions were submitted for review throughout the startup and the beginning of data collection. These changes included the addition of an instructional video to be shown for collecting hair samples and packing checklists to assist the participants in packaging the collection materials and specimens to be returned to RTI. Other changes consisted of the addition of photographs to the full length instructions and minor changes due to usability test results to both the instructions and questionnaires. A quality control checklist which was used by QA staff for conducting the telephone and in-person audits was developed, submitted, and approved by the IRB. All revisions submitted throughout the study were approved.

IRB renewal for RTI was submitted for full review in August 2002. The IRB reviewed and approved the continuation through an expedited review. This approval sustained the demonstration activities for the remainder of the data collection period. This project resulted in no incidents or adverse reactions.

2.10 Incentive Schedule

The type and duration of data collection activities assumed by the study subjects made it appropriate to consider incentives for the demonstration studies. The schedule of payments was agreed to with U.S. EPA at the outset of the project for budgeting purposes. Incentives were distributed by KN according to the schedule in ***Exhibit 2-11***. There was no negative feedback from study subjects during the course of the 12-month study period; however, some dissatisfaction was express by the 0-1 cohort study subjects in the debriefing questionnaire. Questions and comments from participants were phoned in and arose during phone and in-person audits. For example, one participant phoned to ask if she would be receiving a check before Christmas.

Exhibit 2-11. Incentive Schedule Per Study Subject for Sample Collection Activities

Cohort	Sample Types	Cash Payment	Gift Certificate for Child	Total Payment Value	Cash Payment Distribution by Quarter			
					1	2	3	4
0-1	Urine/ Breast Milk	$210	$0	$210	$30	45	60	75
3-5	Urine/Sock	$135	$25	$160	$25	30	35	45
	Hair/Dust	$70		$70	$15	25	30	
	Tap Water	$60		$60	$15	20	25	
6-8	Saliva/Dust	$135	$25	$160	$25	30	35	45
	Volatile Organic Chemical	$40		$40	$15	25		
	Temp/ Relative Humidity	$40		$40	$15	25		

3

Results and Conclusions

These demonstration studies involved the collection of considerable data ranging from the recruitment and retention of the study subjects to the content of the metaquestionnaires and the condition of the environmental and biological samples. Key objectives were to determine whether remote data collection is feasible and to assess the ability of study subjects to collect environmental and biological samples. To that end, it was not necessary nor the original intention of the task order to analyze all the data that were collected. Therefore for this report, we selected key variables for analysis that essentially examined the degree to which this approach to exposure monitoring is feasible and the extent to which these data collection technologies could be successfully implemented with study subjects. Therefore we present in this report:

- Measures of success in recruiting and retaining study subjects
- Response rates for completion of the study questionnaires and diaries
- Assessments of the success and difficulties in completing the web questionnaires
- Study subjects' willingness to provide a wide range of biological and environmental sample types
- Condition and acceptability of the samples for laboratory analyses
- Timeliness of sample collection.

We requested study subjects to start collecting samples shortly after they received the sampling materials. If the instructions were followed to the letter, most samples would have been returned approximately 7 days from the time that sampling materials were shipped. We recognize that this schedule is somewhat arbitrary and that successful exposure monitoring can allow sample collection schedules that are longer than 1 week. However, in a large scale study in which the sampling materials are to be cleaned and reused, there will be additional project expenses if there is a significant inventory of sampling materials in the field at any given time. As an index of timeliness for this report, we used 7 days or less as the threshold for defining a

sample that was returned in a timely manner.

The condition of the sample upon receipt helps to determine whether or not a sample could be properly identified and analyzed to yield a result that would not be suspect, for whatever reason. These evaluations are discussed below. ***Exhibit 3-1*** summarizes the acceptance criteria used in this study. Although other criteria could be proposed for some of the sample types, those shown in the exhibit were expected to be of greatest concern from the perspective of the desired state of the sample for shipping; the need to link samples to participants; and their importance in a longitudinal exposure study, e.g., sample collection dates/times. Notes were kept for each sample shipment received. Observations included those about samples along with comments about packaging and missing items. General text comments for each shipment are included in ***Appendices K-1, K-2, and K-3*** for the 0-1, 3-5, and 6-8 cohorts, respectively. Data tables generated from the master database used to develop summary statistics for the 0-1, 3-5, and 6-8 cohort are shown in ***Appendices L-1, L-2, and L-3 ,*** respectively.

In accordance with agreements made at the outset of the task order, we have purposely reported the findings for each cohort separately. Additional analyses of the data collected for these cohorts may be beneficial and appropriate as hypotheses for the NCS are finalized. For each cohort we present selected findings that are directed at responding to the study objectives.

3.1 Observations of the 0-1 Cohort

3.1.1 Recruitment and Retention

We started the demonstration study with nine study subjects. As discussed in ***Section 2.3,*** our intent was to include a broad representation of participants in each cohort with regard to household income status, region of country and urban-rural location of home (***Exhibits 2-7*** and ***2-8***). We were successful in recruiting a study subject for each of the nine sampling strata per cohort with two exceptions. We were unable to recruit a study subject for the rural, low income strata and selected a subject from rural medium income group. We were also unable to recruit a rural, high income participant and substituted with a study subject from the west/urban, high income group. The need for these substitutions was driven by two factors: the availability of study subjects in KN's panel and more importantly, the screening criteria we imposed of selecting women who were currently breastfeeding or planning to after birth.

Exhibit 3-1. Criteria for Defining Sample Acceptability

COHORT	SAMPLE MATRIX	SAMPLE ACCEPTABILITY
0-1	Breast milk	Sample received cold Container not leaking Collection date recorded
	Food	Sample received cold Container not leaking Collection date recorded
	Beverage	Sample received cold Container not leaking Collection date recorded
	Urine	Sample observed to be urine Sample received cold Collection date recorded
3-5	Socks	Sample in amber jar Collection date recorded
	Urine	Sample received cold Collection date recorded
	Vacuum dust	Collection date recorded
	Hair	Sample in plastic bag Collection date recorded
	Tap water	Sample received cold Sample not frozen Collection date recorded
6-8	Dust wipe	Sample contained only dust Collection date recorded
	Saliva	Sample received cold Container filled to the mark No evidence of mouthwash Collection date recorded
	VOC badge	Cap properly affixed Badge secured with Teflon tape Badge packaged correctly Collection date recorded
	HOBO (Temp)	HOBO data downloadable HOBO matched temp. data sheet Collection dates recorded

Exhibit 3-2 presents selected statistics regarding the recruitment and retention of study subjects for the 0-1 cohort. Important observations and outcomes for this cohort include the following:

- Of the nine study subjects that started the study in February 2002, seven were still completing questionnaires at the end of the study and six were still providing samples.
- One study subject (mother) dropped out of the study in Month 2 after completing one questionnaire and without providing any samples; sampling shipments were terminated after Month 2. However, KN continued to post the questionnaire. The study subject unexpectedly "re-entered" the study in Months 10, 11, and 12 when metaquestionnaires were completed. A decision to not participate in the demonstration study for several months may have related in part to moving to another home and failing to "reconnect" with KN. Participation was encouraged through a number of telephone calls by KN staff during Month 2 without success.
- Two other study subjects stopped providing samples in Months 7 and 9 of the 12-month study period.
- Although our intent was to start the demonstration study with nine breastfeeding mothers, there were only three that were breastfeeding when data collection commenced in late February 2002. When study subjects were identified and signed consent forms in late 2002, all participants were breastfeeding. The important lesson learned from this aspect of the study is that breastfeeding status can change relatively quickly.
- There were 44 eligible families with children 0 to 1 who were asked to participate. Slightly more than half (54%) agreed to enroll in the study. (Only nine were accepted.) ***Exhibit 3-2*** presents response rates by household income status, but the small numbers limit the conclusions that can be drawn. The lowest response rate was observed for the high income group.
- One of two low income study subjects was not providing samples at the end of the study and two of four middle income participants dropped out of the study. All three high income study subjects finished the study.

Exhibit 3-2. Recruitment and Retention of Study Subjects by Income Characteristic: 0-1 Cohort

Income Characteristic	Recruitment			Retention	
	No. Contacted	No. (%) Agreeing to Participate	No. in Study	No. (%) Completing MetaQx in Month 12	No. (%) Providing Samples in Month 12
Low*	3	2 (67%)	2	2	1
Medium	20	15 (75%)	4	2	2
High	21	7 (33%)	3	3	3
Total	44	24 (54%)	9	7 (78%)	6 (67%)

*Number contacted does not include participant substituted from medium income group.
MetaQx = metaquestionnaire

3.1.2 Web Data Collection: Metaquestionnaire, Food Diary and Debriefing Questionnaire

The questionnaire completion results for the 0-1 cohort are shown in ***Exhibit 3-3***.

Overall, web survey completion for both the metaquestionnaire and food diary was fairly

consistent with an average of seven of eight subjects completing each month. As noted in Section 3.1.1., one subject dropped out of the demonstration study after the first month of data collection. We employed the use of two reminder e-mails and telephone prompting for nonrespondents. Some demonstration participants voiced complaints during the in-person and telephone QA checks that the level of e-mail prompting, while only twice, was excessive. While best practices for self-administered web surveys prescribe a two e-mail approach whereby the first e-mail is a thank-you/reminder prompt, and the second is a prompt for nonrespondents, there may be additional considerations for a longitudinal study with a monthly periodicity that should be investigated for future studies.

Exhibit 3-3. Results of Questionnaire and Food Diary Data Collection: 0-1 Cohort

Questionnaire	Completed (%)
Metaquestionnaires	81 (87/108)
Debriefing (end of study) Questionnaires	100 (8/8)
Food Diary	
Food Diary	81 (87/108)

Metaquestionnaire. The first set of web screens ***(Exhibit 3-4)*** for the metaquestionnaire collected dates for breast milk and urine collection. As described in Section 2.7, soft range and consistency checks were programmed to improve data quality. Overall, study participants were able to record date information for both types of specimen collection.

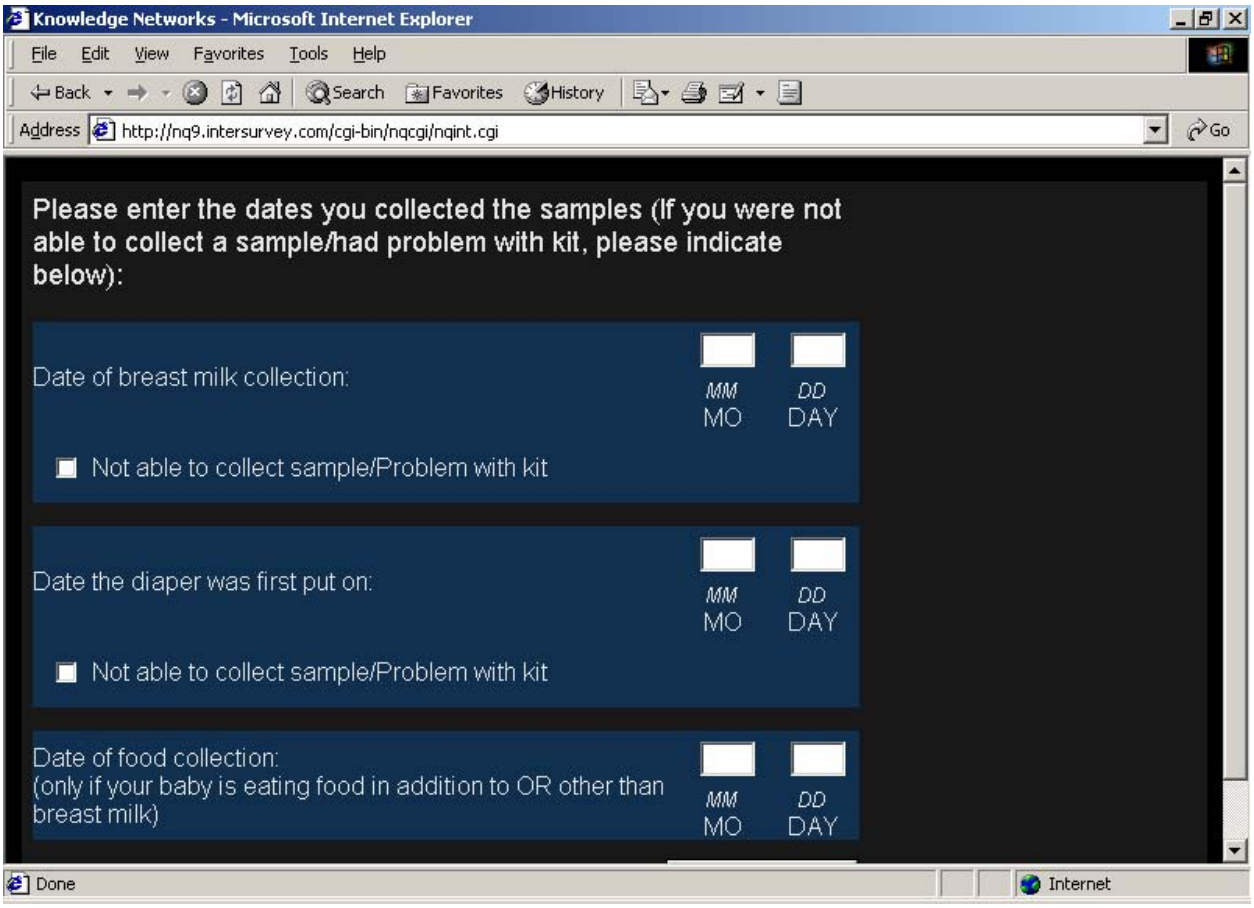
The remainder of the metaquestionnaire was administered to women who were still breast feeding. All of these questions were straightforward and answered by a subset of study participants. These questions gathered information about specific activities conducted in the past month or week by anyone in the household or the mother. We also collected data on whether the mother was taking vitamin supplements or had eaten fish in the past 24 hours. At the end of this section, we collected information related to the child's development.

Food Diary. The food diary was administered to all study participants whose child was consuming solid foods. The diary recorded the food intake for one day and collected the following eight items per food item:

- Meal (e.g. breakfast, lunch, dinner, or snack)
- Name of child's food item

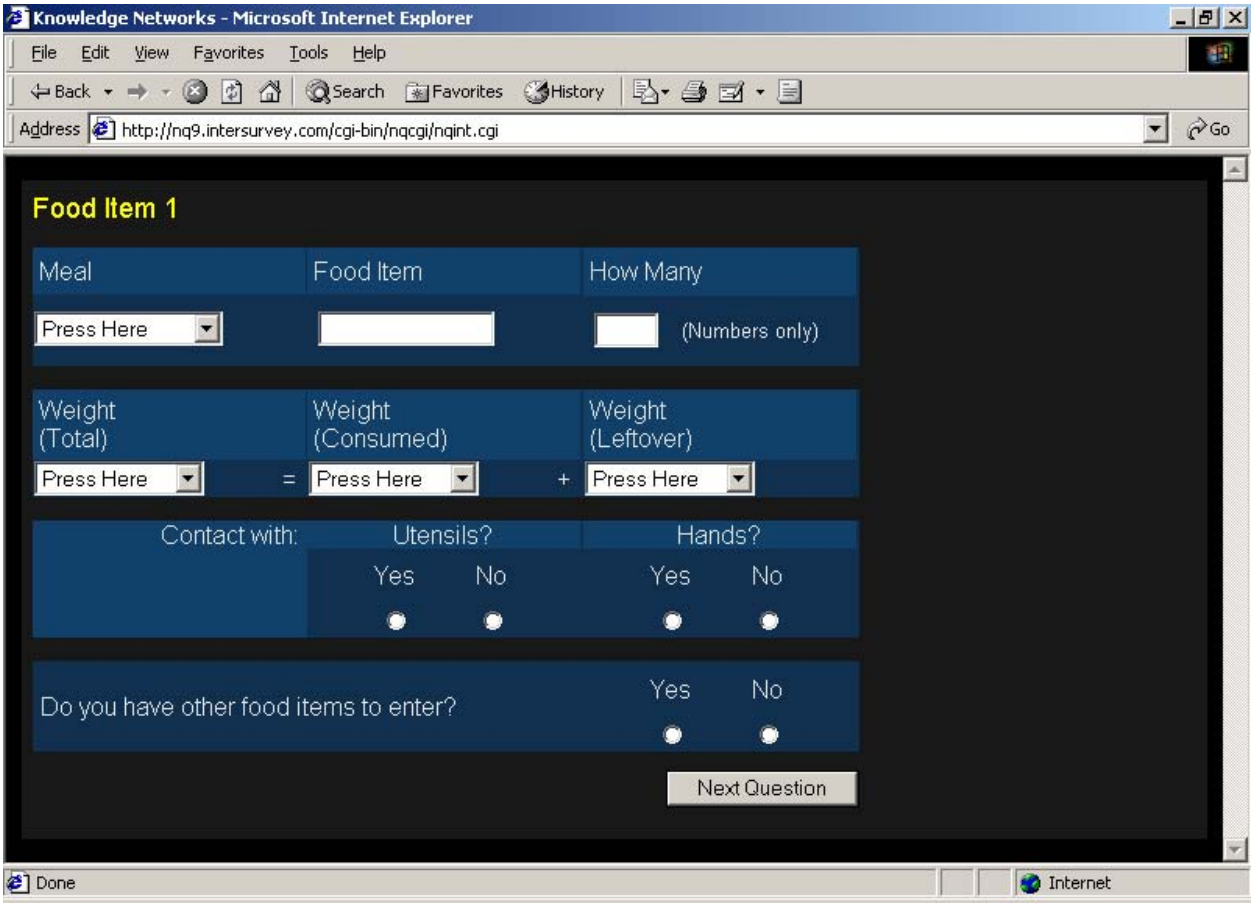
- Quantity of food item
- Weight or volume of food item before handling
- Weight or volume of food item actually consumed by child
- Weight or volume of the leftover
- Contact with utensil
- Contact with preparers' hands

Exhibit 3-4. Web Data Collection for Breast Milk



Study participants recorded eight pieces of information for one food item per web screen. Subjects were prompted to record additional items, and routed to subsequent food diary screens appropriately. See ***Exhibit 3-5***. Overall, this design appears to have worked well. Study participants were able to provide estimates for weight of food consumed and leftover. The validity of these estimates was not verified; follow-up work may be appropriate. The rate of item nonresponse was negligible, and was the result of one participant not answering one of the subitems within one month.

Exhibit 3-5. Web Food Diary



Debriefing Questionnaire. Of the subjects who provided breast milk samples, one indicated that the pump provided in the sampling kit was difficult to use. Additionally, it took about 10 minutes on average for these same subjects to pump the milk into the container provider and store in the freezer.

Study participants did not think it was a problem to collect urine with the special diaper and gauze pad insert, or insert the gauze pad into the container, or store it in their freezer until shipping. Subjects were split equally on whether it was a problem to complete the food diary with about half saying it was "very easy" to "easy" to complete, and others indicating it was "difficult" to "very difficult" to complete. On average, it took 10 minutes to complete the diary. Finally, about 75% of the 0-1 participants indicated it was easy to prepare the duplicate food sample with the remaining 25% noting it was very difficult. About half the subjects indicated that the total incentive amount of $210 was appropriate, and about half indicated it was not.

3.1.3 Environmental Sample Collection: Breast Milk, Beverage, and Food Samples

Exhibit 3-6 shows the results for those participants from whom we were able to collect breast milk, and whether or not samples were provided at each time point. As mentioned previously, all but three participants had stopped breastfeeding by the time data collection commenced. Such a situation would not be anticipated if women were recruited before delivery. Of those three, one participant stopped breastfeeding by the fourth month (June). Of the possible samples, 89% were collected.

An overview of the results for the food and beverage sample collection is shown in ***Exhibits 3-7 and 3-8***. There were a possible 108 participant-months of data collection for the 0-1 cohort, because the research protocol called for 12 months of sampling for the nine study subjects. One participant dropped out of the study during Month 2. Therefore, we used a denominator of 98 participant-months, defined as those months when participants received sample collection materials, for reporting response rates. A total of 83% and 73% of the beverage and food samples, respectively, were collected.

Appendix M-1 shows the masses of food and beverage collected. The data are organized by participant by month. In general, the masses of solid food and beverages consumed were higher for babies that were not breast feeding than those who were. No other analyses have been performed on these data.

3.1.4 Biological Sample Collection: Urine

Taking into account the study subject that essentially withdrew during Month 2, we attempted to collect 98 urine samples (108 possible collections less 10 collections from withdrawn participant). Of these, there were 86 samples (88%) submitted by the participants (***Exhibit 3-9***). The urine samples that were not collected were attributed to the two study subjects that dropped out of the study in Months 7 and 9 when they stopped providing any biological or environmental samples.

Exhibit 3-6. Collection Summary and Condition of Breast Milk Samples: 0-1 Cohort

Part	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
001												
002												
003												
004												
005												
006												
007												
008												
009												

Sample in acceptable condition for analysis. Acceptable sample defined as sample received cold, container was not leaking, and collection date recorded.

Sample in unacceptable condition. Unacceptable sample defined as sample received either warm, container was leaking, or collection date not recorded.

Participant not breast feeding.

No sample collected

Sample Collection Summary	
Mothers breast feeding at outset of study	3
Participant – months of breast milk sample collection[1]	28
Breast milk samples collected	89% (25 samples/28 sampling events)
Acceptable sample rate	88% (22 acceptable samples/25 samples)

[1]Defined as the number of months when the participant was breast feeding

Exhibit 3-7. Collection Summary and Condition of Duplicate Food Samples: 0-1 Cohort

Part	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
001												
002												
003												
004												
005												
006												
007												
008												
009												

Sample in acceptable condition for analysis. Acceptable sample defined as sample received cold, container was not leaking, and collection date recorded.

Sample in unacceptable condition. Unacceptable sample defined as sample received either warm, container was leaking, or collection date not recorded.

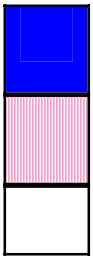
No sample collected

Sample Collection Summary	
Participant-months of food collection[1]	98
Food samples collected	73% (72/98)
Acceptable food samples collected	86% (62/72)

[1] Defined as the number of months when participants received materials to collect a food sample.

Exhibit 3-8. Collection Summary and Condition of Duplicate Beverage Samples: 0-1 Cohort

Part	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
001												
002												
003												
004												
005												
006												
007												
008												
009												



Sample in acceptable condition for analysis. Acceptable sample defined as sample received cold, container was not leaking, and collection date recorded.

Sample in unacceptable condition. Unacceptable sample defined as sample received either warm, container was leaking, or collection date not recorded.

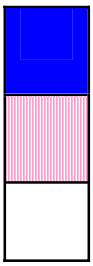
No sample collected

Sample Collection Summary	
Participant-months of beverage collection[1]	98
Beverage samples collected	83% (81/98)
Acceptable beverage samples collected	69% (56/81)

[1] Defined as the number of months when participants received materials to collect a beverage sample.

Exhibit 3-9. Collection Summary and Condition of Urine Samples Received: 0-1 Cohort

Part	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
001												
002												
003												
004												
005												
006												
007												
008												
009												



Sample in acceptable condition for analysis. Acceptable sample defined as sample received cold, contained only urine, and collection date recorded.

Sample in unacceptable condition. Unacceptable sample defined as sample received either warm, container other than urine, or collection date not recorded.

No sample collected

Sample Collection Summary	
Participant-months of urine sample collection[1]	98
Urine samples collected	88% (86/98)
Acceptable urine samples	87% (75/86)
Urine samples with detectable levels of creatinine[2]	100% (22/22)

[1] Defined as the number of months when participants received materials to collect a urine sample.
[2] Defined as the number of urine samples with detectable creatinine per number of samples analyzed.

3.1.5 Indices of Compliance with Study Protocol

Acceptability. Of the breast milk samples collected, 88% were in acceptable condition (i.e., cold, not leaking, and collection date recorded), when they reached the laboratory, as shown in ***Exhibit 3-6***.

For the food and beverage samples, 86% of the food and 69% of the beverage samples were received cold in a non-leaking container with the collection date recorded. These data are shown graphically in ***Exhibits 3-7 and 3-8***. We noted that only one of the study subjects was able to provide duplicate beverage samples in acceptable condition for all 12 months. Consistency was better for the duplicate food samples. Most of the beverage samples were unacceptable because of leakage. This indicates that the samples were not properly frozen before return shipment, the cooling capacity of the blue ice packs was insufficient or they were not properly frozen, or the sample sat outside in the heat and sun prior to FedEx pickup. These problems can be addressed, assuming full compliance with protocols, by more detailed protocols (e.g., freeze samples for at least 24 hours before return shipment) and increased cooling capacity (more ice packs).

A total of 86 urine samples were collected and 75 of these were acceptable ***(Exhibit 3-9)*** for an acceptability rate of 87%. An acceptable sample was one that was received free of feces, cold (if not frozen), in the proper container, and labeled with the collection date. Participants were very good about following instructions with regard to collecting only those samples free of feces. Multiple diapers were provided to be sure that this could be done for each monitoring event. Since contamination of the gauze pads by feces was not a problem, this question, although asked during sample log-in, was not probed specifically in the statistical analysis.

The results of the creatinine analyses are summarized in ***Exhibit 3-9***. Complete data are shown in ***Appendix M-2***. In all cases, creatinine was detected in the urine samples. Two of the measurements made on samples from Month 8 indicated very low values. This suggests very dilute urine, either natural or because of added water. However, it is clear that all of the samples contained urine. Data quality for the creatinine analyses was assessed through the use of lab blanks. Water samples were shipped to Quest Diagnostics to serve as method blanks. Two samples were shipped with Batch 1, and one each with Batches 2 and 3. No creatinine was detected in any of the blank samples.

Timeliness. We looked at the amount of time it took the parents of the 0-1 cohort to return breast milk, food, beverage and urine samples as an index of timeliness for completing the sampling protocol. The timeliness of breast milk sample collection (specified to be within one week of kit receipt) is shown in ***Exhibit 3-10***. A total of 92% of the samples were collected in a timely manner. It is important to recognize that these samples were being provided by three individuals, two of which breastfed the duration of the study. For food and beverage samples, approximately 80% were collected within seven days (***Exhibits 3-11*** and ***12***). Three of nine participants consistently collected their samples in a timely fashion. A total of 81% of the urine samples were collected in a timely manner ***(Exhibit 3-13).***

An important aspect of the demonstration studies was determining the extent to which study subjects complied with the instruction of dating samples and completing metaquestionnaires *after* collecting the samples. We found that study subjects were remarkably compliant these instructions for all categories of the samples collected from the 0-1 cohort. Of all the samples collected, 94% were labeled with a collection date. Of those samples with sample collection and questionnaire completion dates, 96% of the participants completed metaquestionnaires within 1 day of collecting the sample (***Exhibit 3-14***).

Based on comments we received during the quality assurance visits and calls, we expected to find that most participants in the 0-1 cohort were collecting samples on the weekend after they received the kit. Using only those samples in which a date was recorded on the sample received, ***Exhibit 3-15*** indicates that many participants did find the weekend to be a convenient time to collect the urine, food, and beverage samples. However, we were pleased to see that in many instances samples were collected in the middle of the week, presumably soon after the sampling materials were received and in accordance with the instructions. Collectively, slightly more samples were being collected on weekdays and than weekends.

Exhibit 3-10. Timeliness of Breast Milk Sample Collection: 0-1 Cohort

Part	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
001												
002												
003												
004												
005												
006												
007												
008												
009												

Sample collected within 7 days of receipt of collection materials

Sample collection date not provided, but sample was collected

Participant not breast feeding

No samples collected

Sample Collection Summary	
Timeliness rate	92% (23 samples collected within 7 days/25 samples)

Exhibit 3-11. Timeliness of Food Sample Collection: 0-1 Cohort

Part	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
001												
002												
003												
004												
005												
006												
007												
008												
009												

Sample collected within 7 days of receipt of collection materials

Sample collected after 7 days

Sample collection date not provided, but sample was collected

No samples collected

Sample Collection Summary	
Timeliness rate	81% (58 samples collected within 7 days/72 samples)

Exhibit 3-12. Timeliness of Beverage Sample Collection: 0-1 Cohort

Part	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
001												
002												
003												
004												
005												
006												
007												
008												
009												

Sample collected within 7 days of receipt of collection materials

Sample collected after 7 days

Sample collection date not provided, but sample was collected

No samples collected

Sample Collection Summary	
Timeliness rate	79% (64 samples collected within 7 days/81 samples)

Exhibit 3-13. Timeliness of Urine Sample Collection: 0-1 Cohort

Part	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
001												
002												
003												
004												
005												
006												
007												
008												
009												

Sample collected within 7 days of receipt of collection materials

Sample collected after 7 days

Sample collection date not provided, but sample was collected

No samples collected

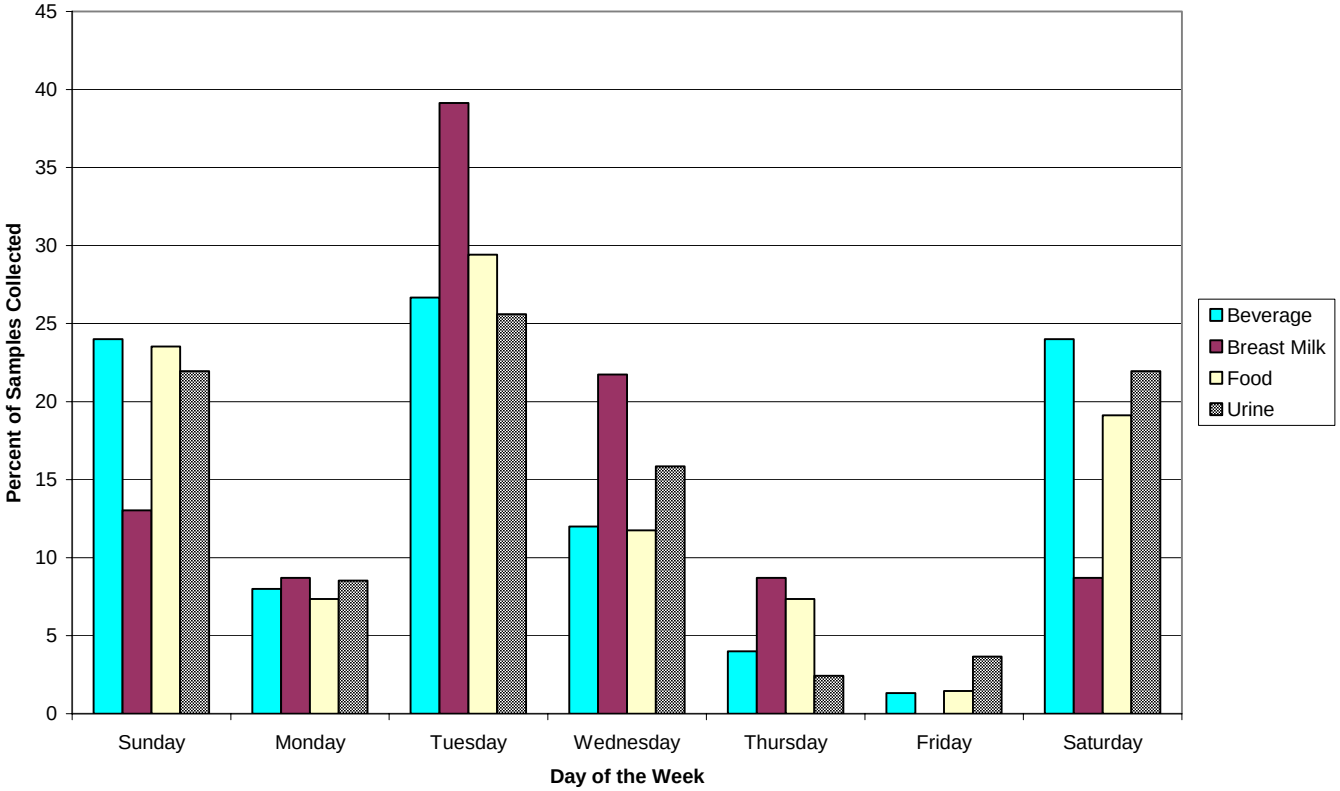
Sample Collection Summary	
Timeliness rate	81% (70 samples collected within 7 days/86 samples)

Exhibit 3-14. Temporality of Sample Collection and Metaquestionnaire Completion by Sample Type: 0-1 Cohort

Type of Sample	Total No. of Samples Collected	Samples Collected with Date Recorded (%)	Samples Meeting Temporality Requirement* (%)
Breast Milk	25	92 (23/25)	100 (23/23)
Food	72	94 (68/72)	94 (64/68)
Beverage	81	93 (75/81)	96 (72/75)
Urine	86	95 (82/86)	96 (79/82)
Total	264	94 (248/264)	96 (238/248)

*Temporality requirement defined as sample was collected same day or day before metaquestionnaire was completed.

Exhibit 3-15. Samples Collected by Day of Week: 0-1 Cohort



3.1.6 Summary and Conclusions: 0-1 Cohort

We started data collection with 3 breast feeding and 6 non-breast feeding participants who were asked to provide metaquestionnaire data, urine, breast milk samples or and duplicate food and beverage samples in each of 12 sampling months. Approximately 45 % of the eligible families that were approached to participate agreed to enroll. Retention over the 12-month study period (6 of 9 still returning samples at end of the study) was not as favorable as hoped for, but this outcome might have been expected given the demands that are placed on mothers with newborns. Participants dropping out of the study came from the low and middle income groups.

Study participants in the 0-1 cohort were generally compliant with what was asked. We observed an 80%+ rate for completing metaquestionnaires and providing samples (***Exhibit 3-16***). The one exception was the duplicate food sample in which 73% of the samples were provided perhaps indicating a level of burden that was different than the other collected samples. This finding may not be surprising when considering that the samples were collected during a busy time of the day and that diet samples, unlike the others, posed an economic burden. However, three-quarters of the participants said in the debriefing survey that the sample was easy to prepare. The remainder said it was very difficult. The debriefing questionnaire also indicated that participants were split equally on the difficulty in completing the accompanying food diary; about one-half said it was easy to very easy.

The majority of samples with the exception of the beverage were in good condition when they were received in the lab. Acceptability rates were 85%+ for breast milk, urine, food; but only 69% of the beverage samples were acceptable. Many were unacceptable because they were warm or leaking or the date was not recorded. Recommendations for additional cooling and clarification of instructions will be necessary to improve the success rates for collecting these types of samples.

The study provided evidence that breast milk can be collected without major difficulties. Special attention needs to be paid to keeping samples cold during return shipment, especially in hot summer months. Stressing the importance of allowing sufficient time for the milk and cold packs to freeze prior to return shipment is important. Recognizing the small number of women in the demonstration study, we were impressed with the overall willingness to provide samples and the condition of the samples when they were received.

Exhibit 3-16. Summary of Data and Sample Collection: 0-1 Cohort

Sample/Data Collection	Percent Compl.[1]	Percent Accept.[2]	Percent with Acceptable Timeliness[3]	Percent with Date Recorded[4]	Percent with Acceptable Temporality[5]	Major Problems/Comments
Breast Milk	89	88	92	92	100	One participant (of three) thought that the pump was difficult to use.
Food	73	86	81	94	94	No significant problems.
Beverage	83	69	79	93	96	One-third of beverage samples were in unacceptable condition (e.g., leakage) upon receipt.
Urine	88	87	81	95	96	No significant problems.
MetaQx[6]	81					No significant problems. Two email prompts to complete the Qx were considered excessive by some participants.
Food Diary	81					

[1] Percent Completed (Number of samples or questionnaires received ÷ total number of possible samples).
[2] Percent Acceptable (Number of samples considered to be acceptable for analyses ÷ total number of samples received). See exhibits and text for definitions of acceptability.
[3] Percent with Acceptable Timeliness (Number of samples received within 7 days of kit shipment ÷ total number of samples received).
[4] Percent with Date Recorded (Number of samples with date properly recorded ÷ total number of samples received).
[5] Percent with Acceptable Temporality (Number of samples collected same day or day before meta questionnaire completed ÷ total number of samples collected with date recorded).
[6] MetaQx (Metaquestionnaire)

Generally, the participants were timely in collecting samples after kits were sent (at least 80% of the collected samples were obtained within 7 days of receiving the kits). As an acceptance criterion, timeliness might not be as important as other aspects of sample collection. However, delays in receiving and recycling sampling equipment is a consideration that may increase equipment and labor costs during field operations.

Parents were found to be compliant with dating the samples (90%+) and completing the metaquestionnaires (90%+) on the same day (or within 1 day) after collecting the sample, as requested. Even with what seems to be a high level of compliance, anything less than 100% will increase the costs of a longitudinal study given the over-sampling and additional materials that would be required to compensate.

A key aspect of this demonstration study was to evaluate the extent to which study subjects, rather than field technicians, could successfully and reliably collect samples if a reduced rate of acceptable samples is acceptable. The data and samples returned, as well as the results of the field visits and calls, indicated that study subjects can successfully collect samples

if carefully instructed. Also, we observed no signs of sample tampering. Diaper insert samples were analyzed for creatinine to confirm that the samples did indeed contain urine. In all analyzed samples, we detected creatinine. With infants, we can anticipate problems with obtaining a "good" sample from diapers, if they become soiled overnight. This might result in a reduced sample expectation for this type of sample.

For the number of samples collected over a 12-month period, the level of burden placed on the 0-1 cohort parents did not appear to be excessive by our own estimates and the information provided by the participants (***Exhibit 3-17***). The fact that samples were generally returned in a condition acceptable for analyses and collected in a timely fashion provides some evidence that the overall level of burden was satisfactory, but as pointed out earlier, we lost one-third of the study subjects in this 12-month study. However, the extent to which participants had difficulties with receiving shipments and returning them was not explored as thoroughly as we would have liked. We know from the quality assurance contacts, that participants occasionally had difficulties with shipping, but we did not quantify these types of problems. A study protocol that places considerable long-term responsibility on the study subjects to monitor receipt of shipments and their return is an important consideration and if not handled properly could affect the overall level of burden and satisfaction.

It is important to note that we received a few negative comments about burden in the debriefing survey (e.g., food diary was difficult to complete and some saying that the duplicate food sample was difficult to prepare) and the quality assurance visits/calls (e.g., "the hardest thing has been the time it takes to track everything"). Also, participants were evenly split on whether the $210 incentive that was offered was adequate; about one-half said that it was not enough.

3.2 Observations of the 3-5 Cohort

3.2.1 Recruitment and Retention

Nine children-parent study subjects were successfully enrolled in the 3-5 cohort. We were able to identify and recruit a study subject for each of the sampling strata discussed previously in ***Exhibit 2-8***. Selected recruitment and retention characteristics for this demonstration study are presented in ***Exhibit 3-18*** and summarized below.

- There were 79 eligible families that were contacted and asked to participate. Of these, 23 (29%) agreed to enroll and nine were selected. The lowest response rate was observed in the high income group (20%).
- Retention rates for this cohort were encouraging. Eight of nine study subjects (89%) were still completing questionnaires and providing samples at the end of the study.
- The one study subject that withdrew stopped providing samples and data midway through the 10-month study period that started in March 2002 (***Exhibit 2-4***).
- One of three low income study subjects was not providing samples or completing metaquestionnaires at the end of the study. All three of the high income and all three of the middle income study subjects finished the study.

Exhibit 3-17. Observations on Level of Burden: 0-1 Cohort

Sample/ Data Collection	Description of Activity	Duration[1] (min)	Level of Difficulty[2]	Participant Comments
Breast Milk	Breast pump provided. One 2-oz sample per month requested. Label sample and store in freezer. Disassemble pump and wash. Package sample for shipment.	10	3	One participant indicated that the pump would not work and it was assembled incorrectly.
Food & Beverage	Collect a second portion of all food and beverage consumed by infant in provided containers for each type of sample. Label sample, store in refrigerator through 12-hour collection period, then freeze. Package sample for shipment.	13 (duplicate diet only) 30[3] combined	1	Three-fourths of the participants thought it was "easy" to prepare the duplicate food sample.
Urine	Urine sample collected on gauze pad (inserted into diaper) that is worn the evening after the day the breast milk sample is collected. Pad from feces-free diaper is placed in provided container, which is stored in freezer until shipped. Blue ice is shipped with urine sample.	5[3]	2	Most participants did not find the urine pad collection to be burdensome.
MetaQx and Food Diary	Questionnaire and food diary are to be completed day after samples are collected using WebTV.	10	4	About one-half of participants thought the food diary was "difficult" to "very difficult" to complete.

[1] Average duration of time (in minutes) to complete sample activity as reported by sample participants during debriefing, unless otherwise noted.
[2] RTI estimate of level of difficulty; Scale of 1 – 5, with 1 = easy and 5 = difficult.
[3] RTI estimate of duration

Exhibit 3-18. Recruitment and Retention of Study Subjects by Income Characteristic: 3-5 Cohort

Income Characteristic	Recruitment			Retention	
	No. Contacted	No. (%) Agreeing to Participate	No. in Study	No. (%) Completing MetaQx in Month 10*	No. (%) Providing Samples in Month 10*
Low	27	8 (30%)	3	2	2
Medium	22	9 (41%)	3	3	3
High	30	6 (20%)	3	3	3
Total	79	23 (29%)	9	8 (89%)	8 (89%)

*Month 10 = Last month of data collection for this cohort (See Exhibit 2-4).
MetaQx = metaquestionnaire

3.2.2 Web Data Collection: Metaquestionnaire, Activity Diary, and Debriefing Questionnaire

The questionnaire and diary completion results for the 3-5 cohort are shown in ***Exhibit 3-19*** below. Overall, web survey completion for the metaquestionnaires and diary was high, ranging from 89 to 96% complete each survey period across the various instruments.

Urine Metaquestionnaire. The urine questionnaire was administered four times through out the 12-month demonstration period. It captured information on seven questions in addition to date and time for urine and sock sample collection. Overall, the level of item nonresponse per question was negligible. To facilitate reporting which pesticides were applied in the home, we used still images to help the subject find the EPA regulation number on the back of a pesticide product. As shown in ***Exhibit 3-20***, subjects were able to view the location of an EPA regulation number on a bottle, and enter the numbers into the web survey. They were also able to click and expand the still image, as shown in ***Exhibit 3-21***.

Sock Activity Diary. The sock activity diary ***(Exhibit 3-22)*** was scheduled for four, but inadvertently administered only three times (months 2, 5 and 8), throughout the 12-month study demonstration field period. KN did not field the sock diary on the final sampling month. This event points out a difficulty that is a concern in complex surveys but can be overcome with additional oversight processes. The sock activity diary asked about the activities the child participated in while wearing the socks during a 2-hour period on the same day in which the urine sample was collected. Overall study participants were able to provide information for each component of the diary; item nonresponse was negligible.

Exhibit 3-19. Results of Questionnaire and Diary Collection: 3-5 Cohort

Questionnaire	Completed (%)
Urine	92 (33/36)
Hair and Dust	89 (24/27)
Tap Water	89 (24/27)
Debriefing Questionnaire	89 (8/9)
Diary	
Sock Activity Diary	96 (26/27)

Exhibit 3-20. Pesticides Applied in Home

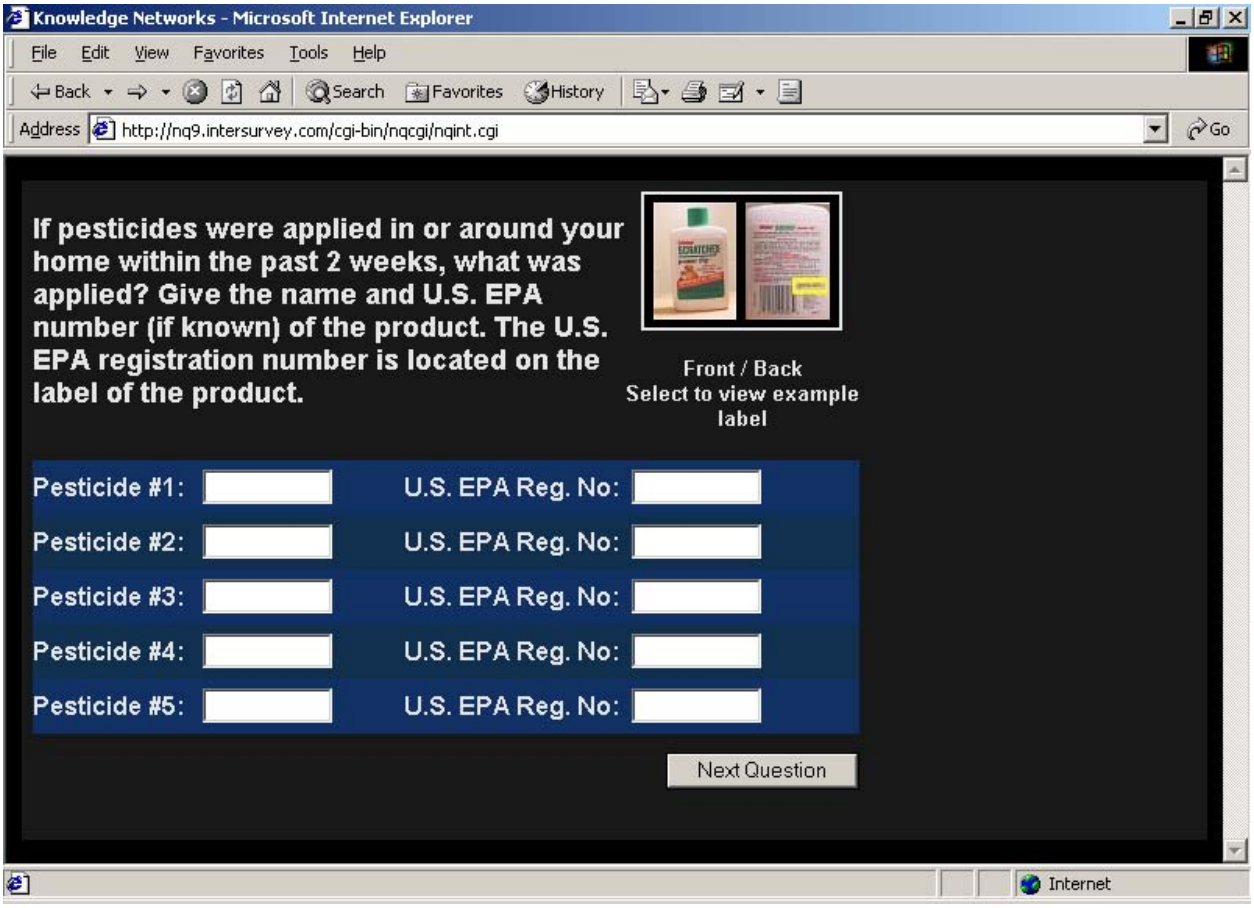
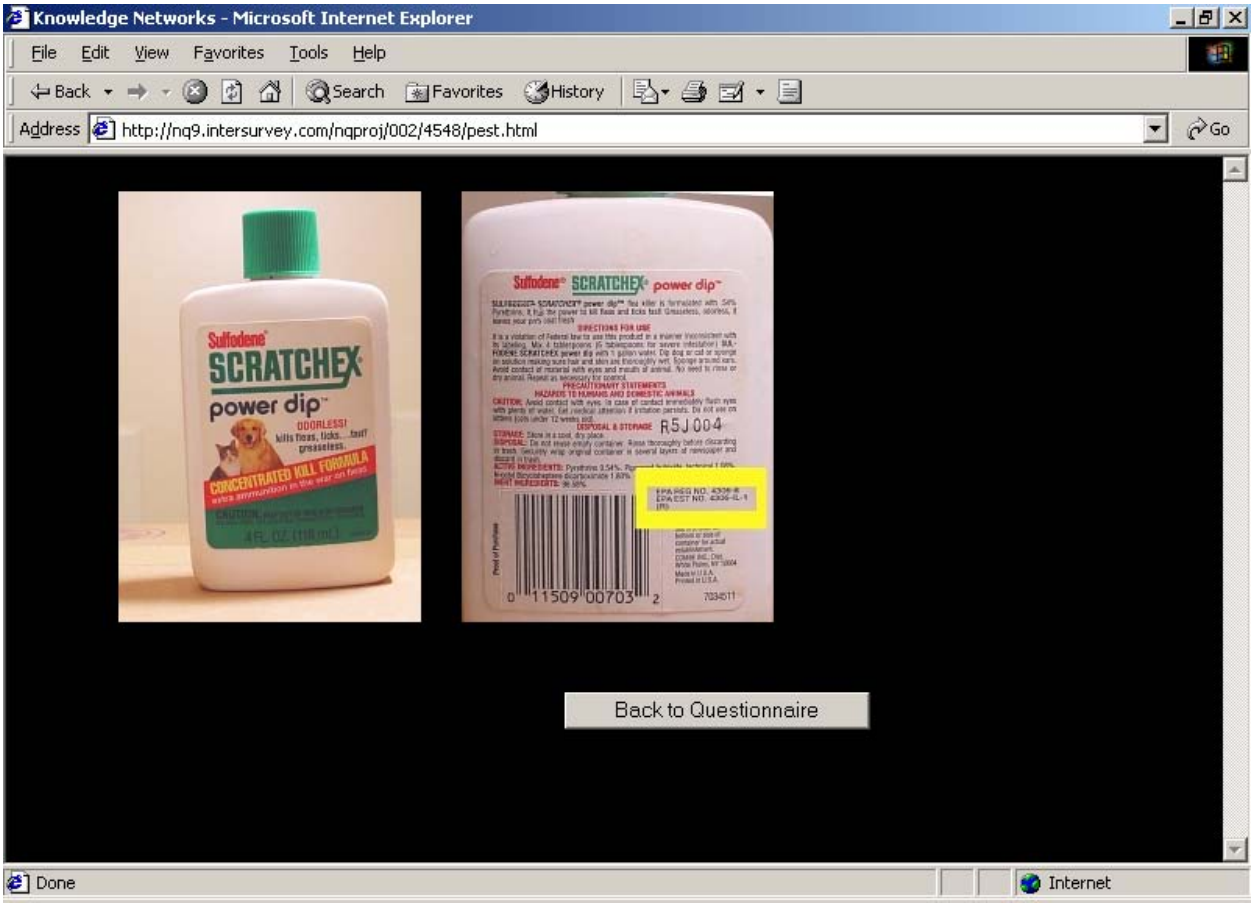


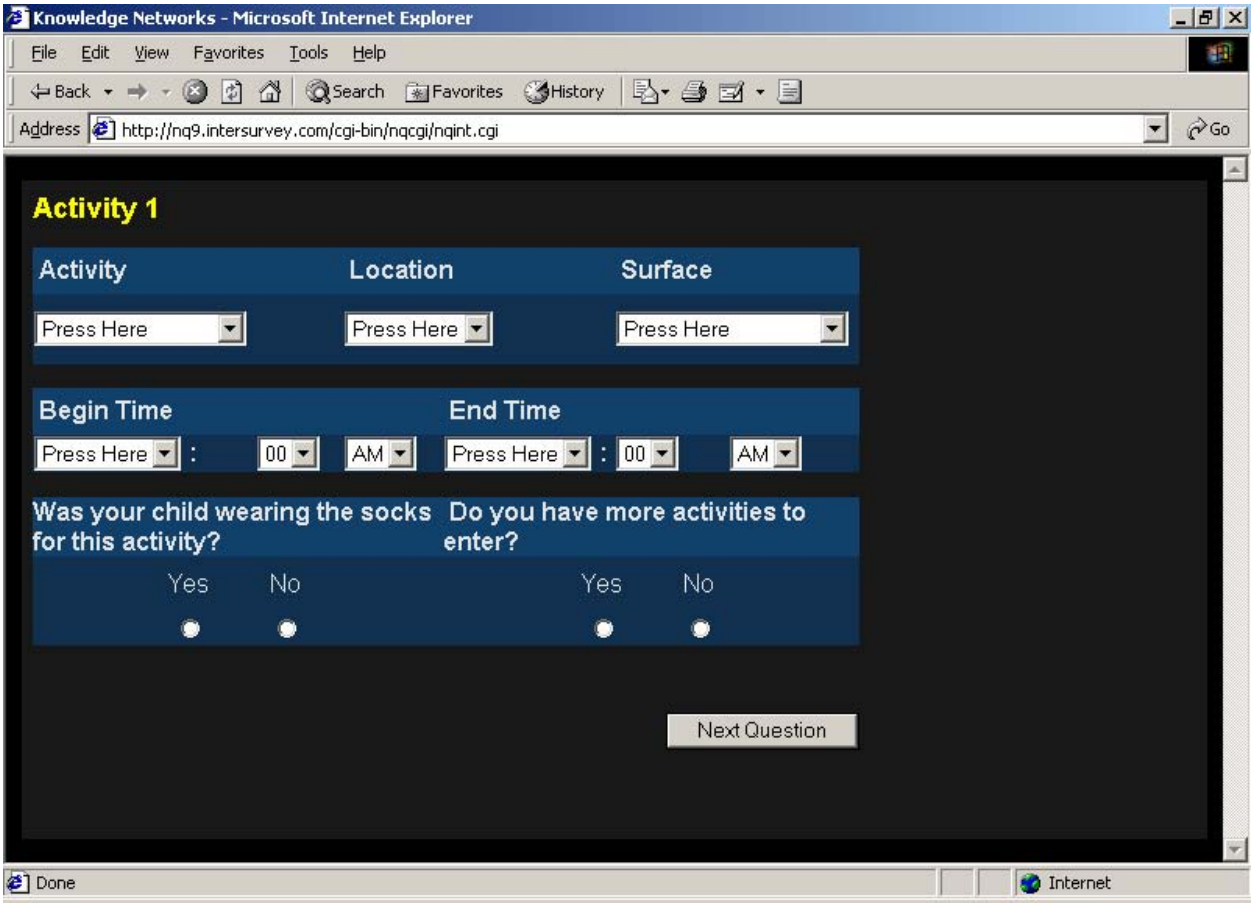
Exhibit 3-21. Still Image of Pesticide Label



Hair and Dust Metaquestionnaire. The hair and dust metaquestionnaire was administered three times throughout the 12-month study demonstration field period. A total of six questions were administered. Overall item nonresponse for this web survey was negligible. In one question, see ***Exhibit 3-23*** below, subjects were asked to indicate the rooms of the house in which they last vacuumed. All subjects who vacuumed in the past 24 hours were asked this question about which room they last vacuumed.

Tap Water Metaquestionnaire. The tap water metaquestionnaire was administered three times throughout the 12-month study demonstration field period. A total of four questions were administered. Overall item nonresponse for this web survey was negligible. In one question, see ***Exhibit 3-24*** below, subjects were asked to indicate the source of tap water in their home. All but one subject was able to identify the source of their water supply.

Exhibit 3-22. Sock Activity Diary Screen



Debriefing Questionnaire. Based on the debriefing survey, seven of eight study participants indicated that it was not a problem to collect the first morning urine from their child. On average it took three minutes to prepare the urine specimen for the freezer.

Five of the eight study participants or 63% indicated that it was a small problem for them to get their child to wear the socks for a 2-hour period. The remaining three indicated it was not a problem. Our QA checks indicated that one child reported the socks were itchy. On average it took four minutes to prepare and package the cotton socks.

Overall, study participants reported that it was not a problem to collect the vacuum cleaner dust, although one subject indicated it was a significant problem. On average it took seven minutes to collect the dust sample. Similarly, seven subjects also reported that it was not a problem to collect the hair sample or bundle the strands of hair together. Only one participant reported difficulty with both. On average it took four minutes to collect and bundle the hair sample. No problems were reported in collecting or testing the water sample in the debriefing survey.

Exhibit 3-23. Room Vacuum Cleaner Was Used

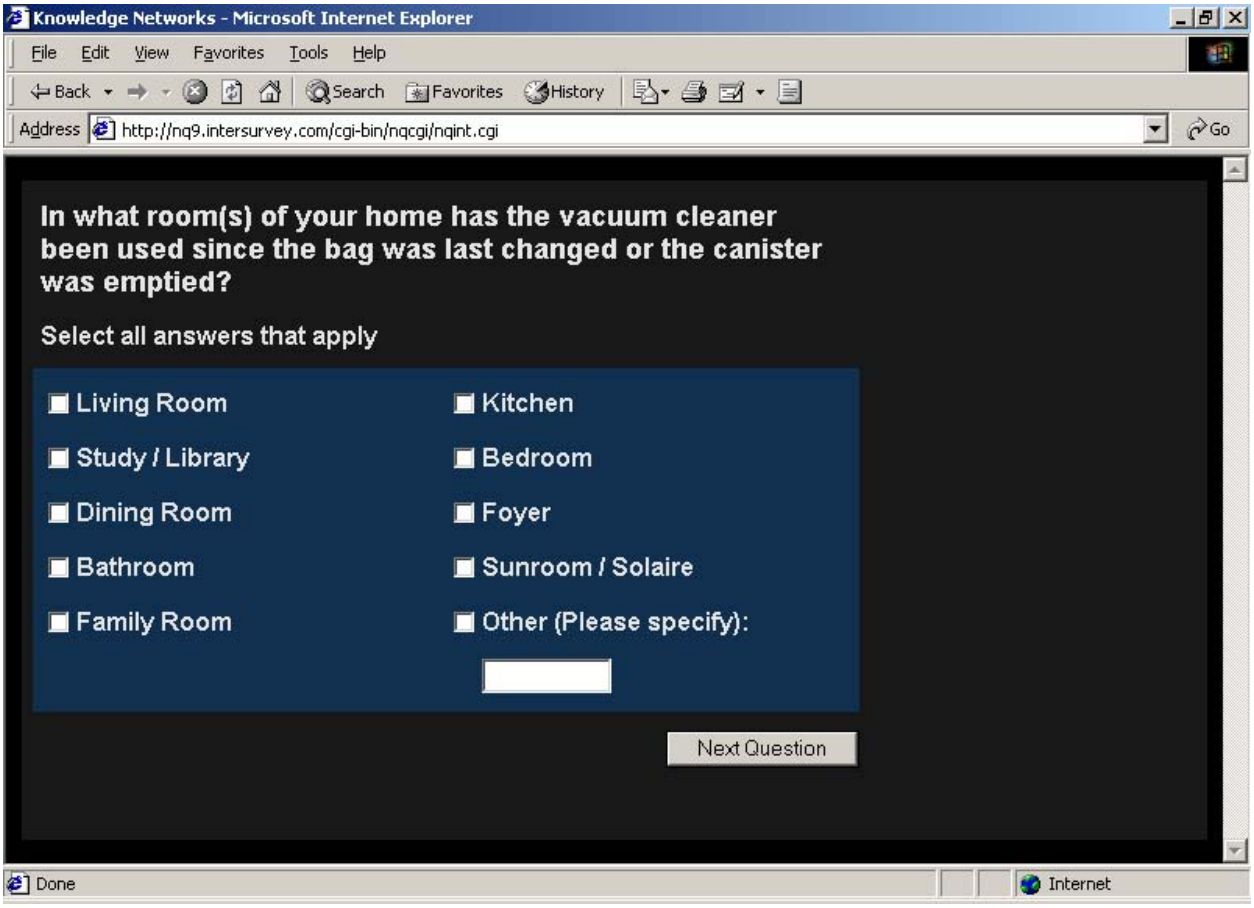
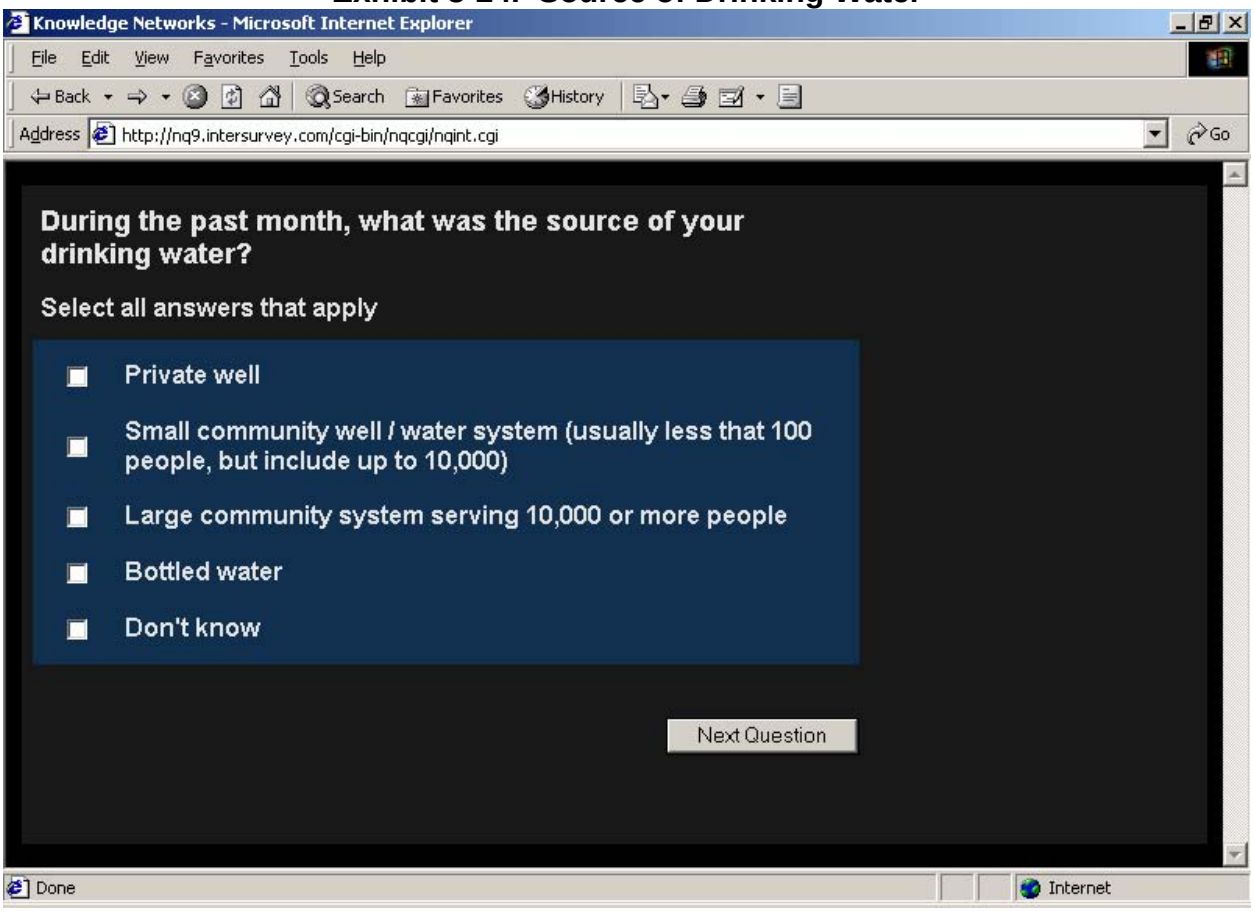


Exhibit 3-24. Source of Drinking Water



3.2.3 Environmental Sample Collection: Cotton Socks, Vacuum Dust, and Tap Water

Exhibit 3-25 shows the number of kits shipped and the number of kits returned. One study subject dropped out halfway through the study. Out of a possible 90 sample sets, 85 were returned for a response rate of 94%. Collection results for socks, vacuum dust, and tap water are shown in ***Exhibits 3-26, 3-27, 3-28*** respectively. The collection rate for socks was 92%; the collection rate for vacuum dust was 96%; and the collection rate for tap water was 93%.

The pH values measured by the participants and by RTI staff upon receipt of the tap water sample are shown in ***Appendix M-3***. In almost all cases, the pH value was lower that that recorded by the participant. Small changes, e.g., half a pH unit, could be attributed to shifts during shipment, especially as carbon dioxide dissolved into the water because of the head space in the bottle. The pH values were recorded after the samples had warmed to room temperature. The impact of sample storage on pH was not investigated using controlled laboratory experiments. Large pH differences could be due to the type of water collected (different amounts of organic matter, etc.) or difficulty experienced by the participant in reading the color of the pH test strips. Each strip had three indicating regions and the color of each segment was to be compared to a standard chart provided with the sample. An inability to distinguish colors could have hampered this test.

3.2.4 Biological Sample Collection: Urine and Hair

Collection response rates for urine and hair ***(Exhibit 3-29 and 3-30)*** were 86% and 96%, respectively. The lower rate of collection for urine is consistent with some of the participants indicating, in the QA visits and calls, that some children did not cooperate and failed to provide urine samples.

3.2.5 Indices of Compliance with Study Protocol

Acceptability. The acceptability of the samples collected was also evaluated. For socks, ***Exhibit 3-26*** shows that of the samples collected, 97% were considered to be acceptable (i.e., received in proper condition and collection date recorded). For the corresponding urine samples ***(Exhibit 3-29)***, the acceptability (i.e., received cold and the collection date recorded) rate was 90%. Additional cooling capacity and a clarification of pre-shipment freezing durations to study subjects would help improve this situation.

Exhibit 3-25. Sample Collection – 3-5 Cohort: All Sample Types

Part	Mar[1]	Apr[2]	May[3]	Jun[1]	Jul[2]	Aug[3]	Sep[1]	Oct[2]	Nov[3]	Dec[1]
010										
011										
012										
013										
014										
015										
016										
017										
018										

[1]Socks and Urine Kit
[2]Vacuum Dust and Hair Kit (October kits sent September 20; November kits sent October 28; December kits sent November 25; See Exhibit 2-4.)
[3]Tap Water Kit

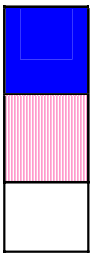
Participant returned kit.

No kit returned.

Sample Collection Summary	
Total number of kits shipped	90
Total number of kits returned	85
Return sample rate	94% (85 returned kits/90 shipped kits)

Exhibit 3-26. Collection Summary and Condition of Sock Samples: 3-5 Cohort

Part	Mar	Jun	Sep	Dec
010				
011				
012				
013				
014				
015				
016				
017				
018				



Sample in acceptable condition for analysis. Acceptable sample defined as sample received in proper container and collection date recorded.

Sample in unacceptable condition. Unacceptable sample defined as either sock sample not received in the proper container or collection date not recorded.

No sample collected

Sample Collection Summary	
Participant-months of sock collection[1]	36
Sock samples collected	92% (33/36)
Acceptable sock samples collected	97% (32/33)

[1] Defined as the number of months when participants received materials to collect a urine and sock sample.

Exhibit 3-27. Collection Summary and Condition of Vacuum Dust Samples: 3-5 Cohort

Part	Apr	Jul	Oct
010			
011			
012			
013			
014			
015			
016			
017			
018			

Sample in acceptable condition for analysis. Acceptable sample defined as sample collection date recorded.

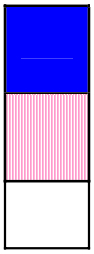
No sample collected

Sample Collection Summary	
Participant-months of vacuum dust collection[1]	27
Vacuum dust samples collected	96% (26/27)
Acceptable vacuum dust samples collected	100% (26/26)

[1] Defined as the number of months when participants received materials to collect samples.

Exhibit 3-28. Collection Summary and Condition of Tap Water Samples: 3-5 Cohort

Part	May	Aug	Nov
010			
011			
012			
013			
014			
015			
016			
017			
018			



Sample in acceptable condition for analysis. Acceptable sample defined as sample received cold, not frozen, container not leaking, and collection date recorded.

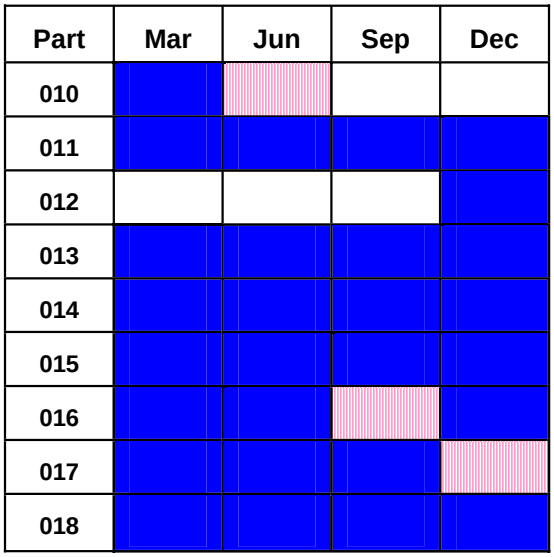
Sample in unacceptable condition. Unacceptable sample defined as either water sample not received cold, not received frozen, container was leaking, or collection date not recorded.

No sample collected

Sample Collection Summary	
Participant-months of tap water collection[1]	27
Tap water samples collected	93% (25/27)
Acceptable tap water samples collected	88% (22/25)

[1] Defined as the number of months when participants received materials to collect samples.

Exhibit 3-29. Collection Summary and Condition of Urine Samples: 3-5 Cohort



Sample in acceptable condition for analysis. Acceptable sample defined as urine sample received cold and collection date recorded.

Sample in unacceptable condition. Unacceptable sample defined as either urine sample not received cold or collection date not recorded.

No sample collected

Sample Collection Summary	
Participant-months of urine collection[1]	36
Urine samples collected	86% (31/36)
Acceptable urine samples collected	90% (28/31)
Urine samples with detectable levels of creatinine[2]	100% (23/23)

[1] Defined as the number of months when participants received materials to collect a urine sample.
[2] Defined as the number of urine samples with detectable creatinine per number of samples analyzed.

Exhibit 3-30. Collection Summary and Condition of Hair Samples: 3-5 Cohort

Part	Apr	Jul	Oct
010			
011			
012			
013			
014			
015			
016			
017			
018			

Sample in acceptable condition for analysis. Acceptable sample defined as sample received in proper container and collection date recorded.

No sample collected

Sample Collection Summary	
Participant-months of hair collection[1]	27
Hair samples collected	96% (26/27)
Acceptable hair samples collected	100% (26/26)

[1] Defined as the number of months when participants received materials to collect samples.

Creatinine ***(Exhibit 3-29)*** was measured in all of the urine samples. The complete data set is shown in ***Appendix M-4***. Water samples were sent to Quest Diagnostics to serve as method blanks. Two samples were shipped with Batch 1, and one each with Batches 2 and 3. No creatinine was detected in any of the blank samples. In order to assess repeatability, two urine samples from this cohort were split and samples differed by less than 4% of the first measurement obtained.

Acceptability of the vacuum dust samples was 100%, as shown in ***Exhibit 3-27***. Since these samples did not need to be cooled and were solid to begin with, this matrix presented few problems. Comparable acceptability rates (100%) were seen for hair ***(Exhibit 3-30)***.

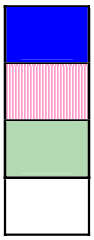
The acceptability of tap water samples, shown in ***Exhibit 3-28***, was 88%. Three of 25 samples were leaking when received. However, all samples were cold when they reached the laboratory. The larger volume, and increased heat capacity, of the water samples likely contributed to their remaining cold. This supports the need for additional cooling capacity in shipments containing urine samples.

Timeliness. Data for socks and urine are shown in ***Exhibits 3-31 and 3-32***, respectively. It is interesting to note that a timeliness rate of 85% was achieved for socks, but a 77% rate was achieved for urine samples. The variation in time between the collection of socks and the collection of urine was not investigated. Such a time difference could be reflective of the cooperation of this age group to provide urine samples. In addition, the needs for first morning void could easily be forgotten by children aged 3-5 years; they could easily get up and go to the bathroom before the parent can intervene. Delays between the collection of an environmental sample and the corresponding biological sample can make studies difficult if the temporal linkage of samples is critical to success.

The timeliness rates for vacuum dust and hair were 81% and 85%, respectively as shown in ***Exhibit 3-33*** and ***3-34***. It was evident that at least one study subject in April did not comply with the instructions that the dust and hair samples be collected on the same day. Whether or not this was true for sets where both types were collected outside the 7 day time frame was not evaluated. The timeliness data for the collection tap water is shown in ***Exhibit 3-35***. For these samples, 84% of the samples were collected on time. It is noted that two study subjects tended to be late across all sample types.

Exhibit 3-31. Timeliness of Socks Sample Collection: 3-5 Cohort

Part	Mar	Jun	Sep	Dec
010				
011				
012				
013				
014				
015				
016				
017				
018				



Sample collected within 7 days of receipt of collection materials

Sample collected after 7 days

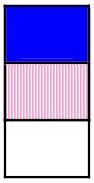
Sample collection date not provided, but sample was collected

No samples collected

Sample Collection Summary	
Timeliness rate	85% (28 samples collected within 7 days/33 samples)

Exhibit 3-32. Timeliness of Urine Sample Collection: 3-5 Cohort

Part	Mar	Jun	Sep	Dec
010				
011				
012				
013				
014				
015				
016				
017				
018				



Sample collected within 7 days of receipt of collection materials

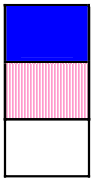
Sample collected after 7 days

No samples collected

Sample Collection Summary	
Timeliness rate	77% (24 samples collected within 7 days/31 samples)

Exhibit 3-33. Timeliness of Vacuum Dust Sample Collection: 3-5 Cohort

Part	Apr	Jul	Oct
010			
011			
012			
013			
014			
015			
016			
017			
018			



Sample collected within 7 days of receipt of collection materials

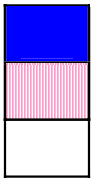
Sample collected after 7 days

No samples collected

Sample Collection Summary	
Timeliness rate	81% (21 samples collected within 7 days/26 samples)

Exhibit 3-34. Timeliness of Hair Sample Collection: 3-5 Cohort

Part	Apr	Jul	Oct
010			
011			
012			
013			
014			
015			
016			
017			
018			



Sample collected within 7 days of receipt of collection materials

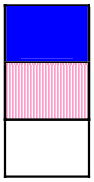
Sample collected after 7 days

No samples collected

Sample Collection Summary	
Timeliness rate	85% (22 samples collected within 7 days/26 samples)

Exhibit 3-35. Timeliness of Tap Water Sample Collection: 3-5 Cohort

Part	May	Aug	Nov
010			
011			
012			
013			
014			
015			
016			
017			
018			



Sample collected within 7 days of receipt of collection materials

Sample collected after 7 days

No samples collected

Sample Collection Summary	
Timeliness rate	84% (21 samples collected within 7 days/25 samples)

For the 3-5 cohort, nearly all (140 of 141 or 99%) of the collected samples across all sample types were dated (***Exhibit 3-36***). Temporality requirements of completing the metaquestionnaire within 1 day of collecting the sample also revealed surprisingly favorable results with 138 of 140 samples (99%) being compliant with the instructions.

Participants in the 3-5 cohort preferred to collect samples on weekdays, shortly after the kits arrived (***Exhibit 3-37***). There was considerably more weekday sample collection than weekend.

3.2.6 Summary and Conclusions: 3-5 Cohort

The data collection period for the 3-5 year old cohort started with nine participants, but the recruitment rate for this cohort was low. Of the eligible families contacted, only 30% agreed to participate. On the other hand, the retention rate was very good. Only one participant from the low income strata dropped out, mid-way through the study. The data and sample collection demands were significant because the participants were asked to collect a variety of samples that cycled over a 10-month period (***Exhibit 2-4***). Response rates for completing the metaquestionnaires for each of the monthly sampling events (e.g., urine and socks, vacuum dust and hair, and tap water) were very good (~90% or better).

Participants were also generally compliant with providing samples (90%+), although urine samples were returned 86% of the time, which was impressive but slightly less than the excellent response rate for the other sample types (***Exhibit 3-38***). This finding may be indicating that first morning void samples, which require cooperation from the child, may be more difficult to collect than some of the other samples. However, most of the parents indicated in the debriefing survey that collection of the urine sample was not a problem. Creatinine was detected in all of the tested samples indicating that participants were providing urine.

Interestingly, we saw two data collection sets (i.e., dust and hair; tap water) in which the response rate was higher for returning the samples (>90%) than for completing the questionnaire (<90%), possibly indicating that there were a few instances in which study subjects forgot or were unable to complete the questionnaire after collecting the samples. Additional follow-up and analyses of the data are appropriate to better understand these study dynamics and the unusual finding for the urine and socks sampling in which there was a higher response rate for metaquestionnaire completion (96%) than for the submission of samples (92%).

Exhibit 3-36. Temporality of Sample Collection and Metaquestionnaire Completion by Sample Type: 3-5 Cohort

Type of Sample	Total No. of Samples Collected	Samples Collected with Date Recorded (%)	Samples Meeting Temporality Requirement* (%)
Socks	33	97 (32/33)	100 (32/32)
Urine	31	100 (31/31)	94 (29/31)
Vacuum Dust	26	100 (26/26)	100 (26/26)
Hair	26	100 (26/26)	100 (26/26)
Tap Water	25	100 (25/25)	100 (25/25)
Total	141	99 (140/141)	99 (138/140)

*Temporality requirement defined as sample was collected same day or day before metaquestionnaire was completed.

Exhibit 3-37. Samples Collected by Day of Week: 3-5 Cohort

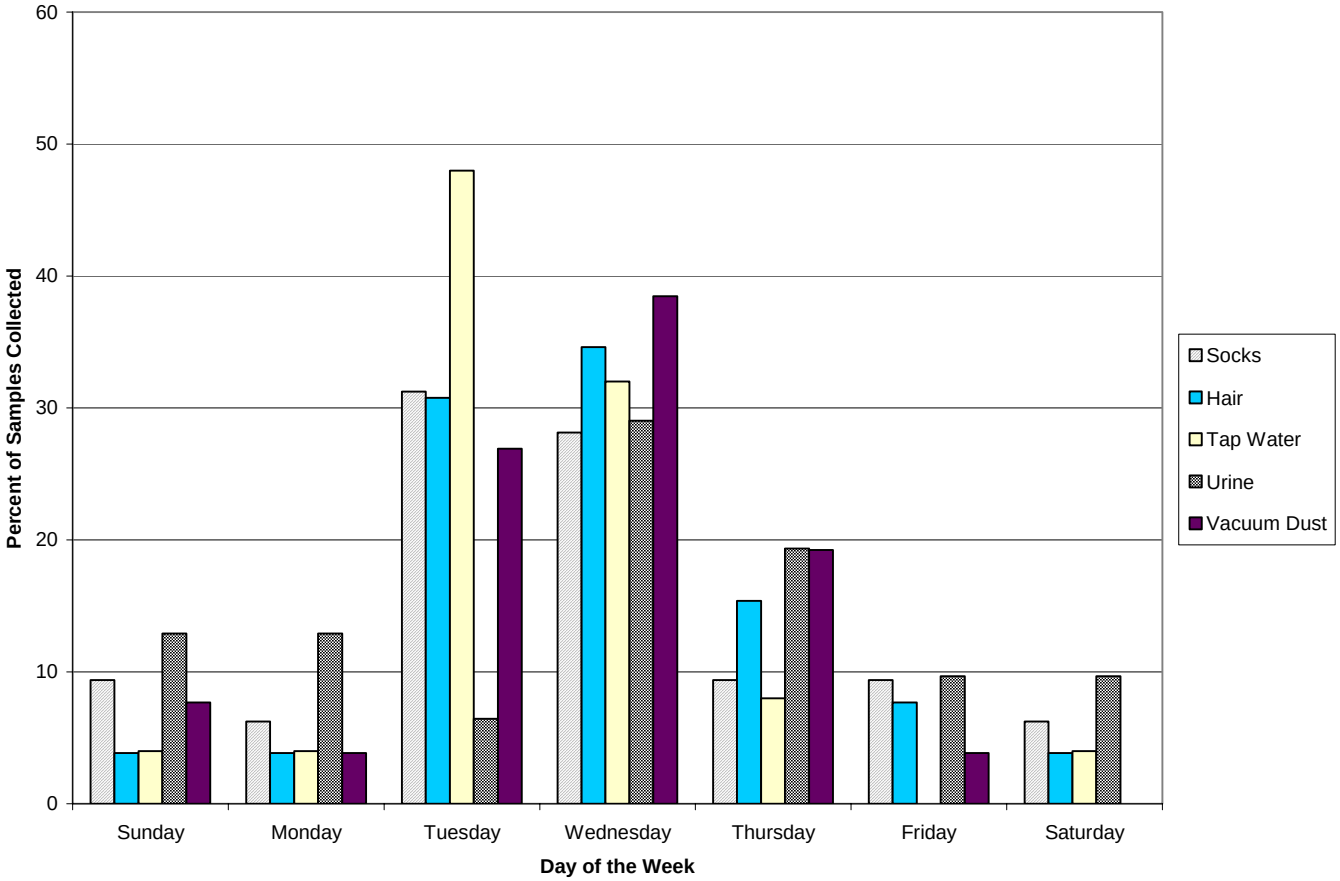


Exhibit 3-38. Summary of Data and Sample Collection: 3-5 Cohort

Sample/Data Collection	Percent Compl.[1]	Percent Accept.[2]	Percent with Acceptable Timeliness[3]	Percent with Date Recorded[4]	Percent with Acceptable Temporality[5]	Major Problems/Comments
Urine	86	90	77	100	94	No significant problems.
Socks	92	97	85	97	100	Some resistance from several children to wear socks for full 2-hour period.
Vacuum Dust	96	100	81	100	100	Only one parent reported difficulty collecting sample.
Hair	96	100	85	100	100	Only one parent reported difficulty collecting sample.
Tap Water	93	88	84	100	100	Leaking containers.
MetaQx: Urine	92					No significant problems.
MetaQx: Hair & Dust	89					
MetaQx: Tap Water	89					
Sock Activity Diary	96					

[1] Percent Completed (Number of samples or questionnaires received ÷ total number of possible samples).
[2] Percent Acceptable (Number of samples considered to be acceptable for analyses ÷ total number of samples received). See exhibits and text for definitions of acceptability.
[3] Percent with Acceptable Timeliness (Number of samples received within 7 days of kit shipment ÷ total number of samples received).
[4] Percent with Date Recorded (Number of samples with date properly recorded ÷ total number of samples received).
[5] Percent with Acceptable Temporality (Number of samples collected same day or day before meta questionnaire completed ÷ total number of samples collected with date recorded).
[6] MetaQx (Metaquestionnaire)

Parents of the 3-5 cohort were also very successful in returning samples that were suitable for analyses (88%+). Exceptional assistance was obtained in recording the date on the sampling packages (97%+) and completing the metaquestionnaires shortly after the sample was collected (94%+). For the 3-5 cohort, the timeliness for sample collection (i.e., collecting the sample within 7 days of when the kit was sent) ranged from 77% for urine to 85% for socks and hair. This difference may have been due in part to our selection of 7 days as a cut-off point for defining timeliness. However, additional time might be needed to permit the most flexible scheduling of the collections by the participants. The difficulty in collecting the urine on time might be suggesting that either the sock collections should be repeated if the urine sample is lost or that the temporal linkage should be known and dealt with in data analysis.

We received feedback during the quality assurance interviews and the debriefing survey about vacuum dust collection. One participant stated that it was a big problem to collect the vacuum dust sample. Additional follow-up after the debriefing survey was not possible; however, we are aware that some study subjects had vacuum cleaning systems in their homes that did not involve a dry dust collection. The collection scheme for vacuum dust conveyed to participants will need to be broadened to encompass a range of vacuum cleaner types, including those that use water or a bag-less canister. This does not present an obstacle to sample collection. It could have an impact on limits of detection if only small samples can be collected from water-based collections. In addition, the mode of scrapping can impact the samples. The exact method proposed will depend on the target analytes for that sample. We made adjustments in our procedures and instructions for collecting samples for water-based and bag-less cleaning systems and believe that the demonstration studies indicated that vacuum dust sample collection is feasible in a full scale study.

Tap water was a relatively easy sample to collect, although we found that several samples were leaking when received in the lab. We believe this problem is correctable with modifications in the instructions. An additional factor identified for this sample type is that it was assumed that all participants could differentiate color equally well; the ability to match colors on the pH test strips was critical to this test. In retrospect, there is no basis for this assumption. Any tests incorporated into the NCS should be free of error that is the result of differences in color perceptions among study participants.

The level of burden associated with completing the metaquestionnaires and collection of the samples for the 3-5 cohort appears to have been acceptable (***Exhibit 3-39***). All of the metaquestionnaires could be completed relatively quickly (10 minutes or less) and the samples generally took less than 10 minutes to collect, with the exception of the socks which were to be worn for 2 hours. Parents noted in the debriefing survey and the quality assurance visits that some children did not like wearing the socks (e.g., found them to be “itchy”). One parent thought that collecting the hair sample was difficult, but most parents did not think it was a problem to collect this type of sample. We received no complaints about the incentive which was $265 for the 3-5 cohort members, if all samples were collected. The instructions provided

Exhibit 3-39. Observations on Level of Burden: 3-5 Cohort

Sample/ Data Collection	Description of Activity	Duration[1] (min)	Level of Difficulty[2]	Participant Comments
Urine	Collect first morning urine void in specimen cup. Label sample with date and time, as well as the time of last urination. Store in freezer for 24 hours. Package sample for shipment.	3	2	Participants indicated that it was not a problem to collect the first morning urine from their child.
Socks	Wear socks indoors without shoes for 2 hours, and then place in sample container. Freeze overnight. Package sample for shipment.	3	2	Five of the eight study participants or 63% indicated that it was a small problem for them to get their child to wear the socks for a 2-hour period. The remaining three indicated it was not a problem. One child indicated the socks were itchy.
Hair	Cut a 1-inch section of hair from the scalp of the child (instructional video provided). Place in bag and record date and time. Package sample for shipment.	4	4	Only one participant said that it was a problem to collect the hair sample; most said it was not a problem.
Vacuum Dust	Remove vacuum cleaner bag from vacuum and place in plastic bag. Record date and time on label. Package sample for shipment.	7	2	One participant used a vacuum cleaner with a water filtration system. This participant was individually instructed on how to collect a sample of dust from the vacuum.
Tap Water	Fill bottle to red line with tap water from kitchen sink tap. Test pH of water with pH strip. Record the pH, date and time on the label. Store in refrigerator until shipped. Package sample for shipment.	6	1	No problems noted.
MetaQx and Sock Activity Diary	Questionnaire and sock diary are to be completed day after samples are collected using WebTV.	10	3	Participants were able to provide information for each component of the diary; item nonresponse was negligible. Error messages were mentioned by some participants.

[1] Average duration of time to complete (in minutes) sample activity as reported by sample participant during debriefing; unless otherwise noted.
[2] RTI estimate of level of difficulty; Scale of 1 – 5, with 1 = easy and 5 = difficult.
[3] RTI estimate of duration

with the sampling kits and via WebTV, including the video for collecting the hair sample, appeared to have been read (or viewed) and understood.

3.3 Observations of the 6-8 Cohort

3.3.1 Recruitment and Retention

For the 6-8 cohort demonstration study, we were able to recruit a study subject for each of the sampling strata identified in ***Exhibit 2-8***. Recruitment and retention rates for the 6-8 cohort are presented in ***Exhibit 3-40***. Notable features were the following.

- We approached 87 families about participating in the study; 27 (31%) agreed to participate. Response rates were comparable for all three income strata.
- Eight of nine (89%) study subjects were completing questionnaires and providing samples at the end of the study.
- The one study subject that withdrew stopped providing samples and metadata three-fourths of the way through the study.
- One of three low income study subjects was not providing samples or completing metaquestionnaires at the end of the study. All three of the high income and all three of the middle income study subjects finished the study.

3.3.2 Web Data Collection: Metaquestionnaire and Debriefing Questionnaire

The results for completing the questionnaires for the 6-8 cohort are shown in ***Exhibit 3-41***. Overall, web survey completion for the metaquestionnaires was very high, ranging from 94 to 97% completed each survey period across the various instruments.

Exhibit 3-40. Recruitment and Retention of Study Subjects by Income Characteristic: 6-8 Cohort

Income Characteristic	Recruitment			Retention	
	No. Contacted	No. (%) Agreeing to Participate	No. in Study	No. (%) Completing MetaQx in Month 10*	No. (%) Providing Samples in Month 10*
Low	32	10 (31%)	3	2	2
Medium	31	10 (32%)	3	3	3
High	24	7 (29%)	3	3	3
Total	87	27 (31%)	9	8 (89%)	8 (89%)

*Month 10 = Last month of data collection for this cohort (See Exhibit 2-4).
MetaQx = metaquestionnaire

Exhibit 3-41. Results of Questionnaire Collection: 6-8 Cohort

Questionnaire Results	Completed (%)
Saliva and Dust	97 (35/36)
VOC and HOBO	94 (17/18)
HOBO	94 (17/18)
Debriefing Questionnaires	75 (6/8)

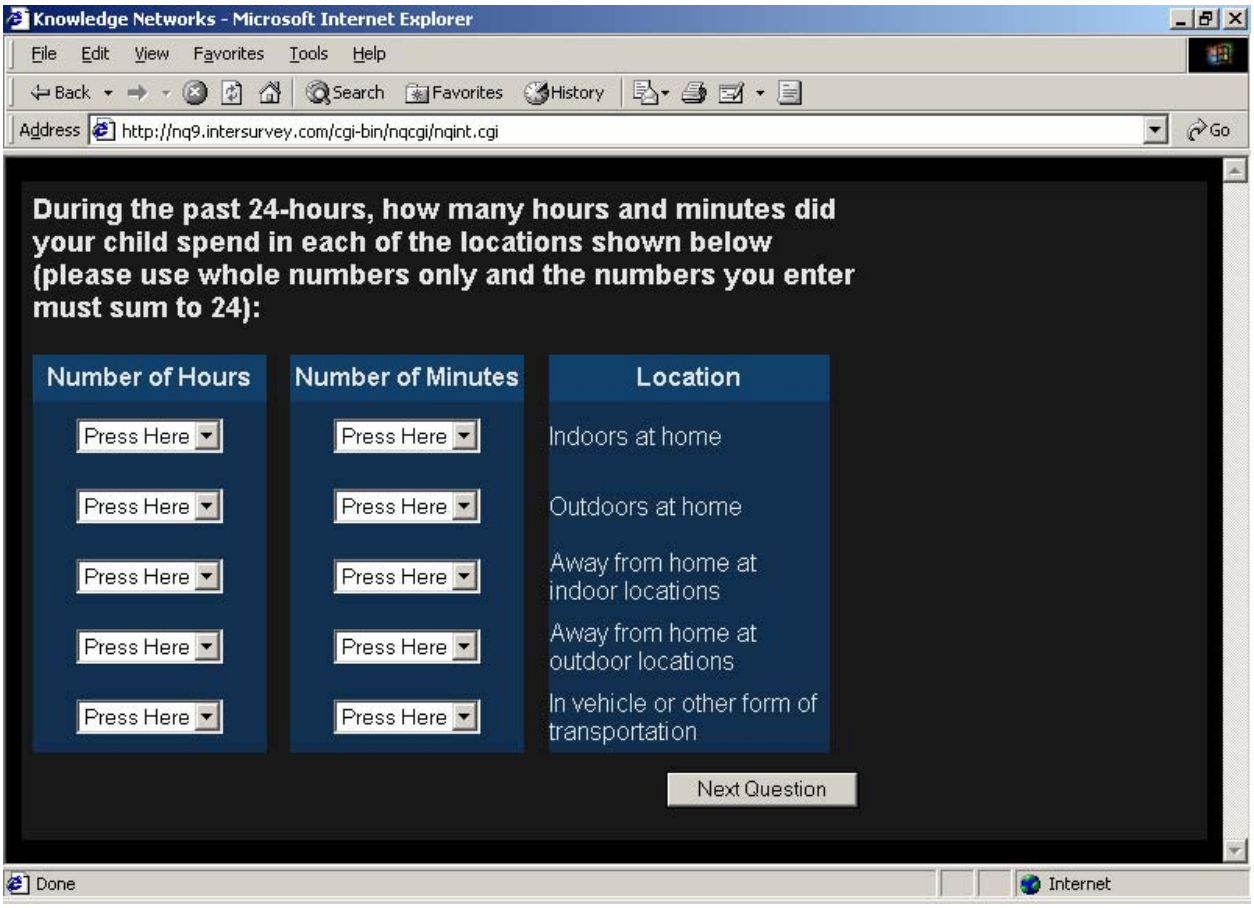
Saliva and Dust, VOC Badge and HOBO (Temperature) Metaquestionnaire.

The periodicity for this questionnaire varied with the collection of the biological or environmental sample collection. Saliva and dust was administered four times; VOC and HOBO were administered twice; and HOBO alone was also administered twice during the 12-month demonstration study field period. This 8-item questionnaire collected information about exposures inside and outside the home. One series of questions in particular sought to collect the number of hours the child spent in various locations during a 24-hour period ***(Exhibit 3-42)***. The collection of hours and minutes per location for the child in a 24-hour period was obtained over several questions and hence web screens. The screen presented in ***Exhibit 3-42*** is an example of the question asked in this series and is the first or initial question asked about hours and minutes in locations. If the subject indicated *any* number of hours or minutes in this screen, subsequent questions specific to that location were asked.

The item nonresponse for this particular item was higher than other web surveys, ranging from 20 to 30%. It was clear that the subjects were having difficulty with the logic checks programmed to ensure the hours reported summed to 24, and that the hours by location were fully accounted. It also appears that they didn't provide an answer in hours or minutes when they found themselves not summing to the hours for a given location.

Asking subjects to account for a full 24-hour period and then further subdividing that time by hours and minutes per location was a cognitively challenging task. This was further complicated by programming logic which produced error messages when the number of hours and minutes did not add up to the 24-hour period. In the future, this data element would benefit greatly from cognitive testing to get a better sense of how to capture these data from subjects.

Exhibit 3-42. Hours and Minutes in Various Locations



Debriefing Questionnaire. Data from the debriefing questionnaire indicated that four study participants did not have a problem with collecting saliva from their child, whereas two reported it was a small problem. On average it took 10 minutes to collect and prepare the saliva specimen. Study participants also noted that it was not a problem to collect the dust sample or to place it in the special shipping container.

Information in the debriefing questionnaire regarding the VOC badge was inconsistent with what we observed in the lab, namely that it was very difficult for study participants to assemble the VOC badges and obtain the cooperation of their child to wear it. The debriefing data were evenly split across three categories ─ not a problem, a small problem, and a big problem ─ to assemble and have their child wear it.

Finally, study participants reported that it was not a problem to setup the HOBO or record the room and outdoor temperature.

3.3.3 Environmental Sample Collection: Dust Wipe, Volatile Organic Compound (VOC) Badge, and HOBO (Temperature)

Exhibit 3-43 shows the number of kits shipped and the number of kits returned. One study subject stopped providing samples in the fourth quarter of the study. Out of a possible 72 sample sets, 70 were returned for a response rate of 97%.

Collection results for settled dust, VOC badges, and HOBOs are shown in ***Exhibits 3-44***, ***3-45, and 3-46***, respectively. The collection rate for dust wipes was 97%; the collection rate for VOC badges was 100%; and the collection rate for HOBO samples was 94%.

3.3.4 Biological Sample Collection: Saliva

Collection results for saliva showed a 97% rate of return ***(Exhibit 3-47)***. This high response rate is consistent with the response rates seen for other samples in which there is direct parental involvement. Also, relative to urine, the collection of saliva is more difficult to forget than is a first morning void.

3.3.5 Indices of Compliance with Study Protocol

Acceptability. For dust wipes, ***Exhibit 3-44*** shows that of the samples collected, 89% were acceptable (i.e., appeared to contain dust and collection date recorded). For the corresponding saliva samples ***(Exhibit 3-47)***, the acceptability rate (i.e., received cold, filled to the red line, contained no mouthwash, and the collection date recorded) was 23%. Saliva was the most problematic sample type, despite its seemingly easy collection. The unacceptable samples were received warm, did not contain the requested volume, or contained the mouthwash that was supposed to be used only to rinse out the mouth *prior* to saliva collection. Some samples were received warm; additional cooling capacity and a clarification of pre-shipment freezing durations would help this situation. The volume requirements should be defined to be larger than what is actually needed to ensure that sufficient sample is collected. The presence of mouthwash in the sample suggests that the instructional materials, although clear in our minds, were not followed. This would need to be presented in stronger terms and some supplemental instructions, such as a video, might be needed. Discarding the first few saliva "deliveries" prior to the collection of the sample to be analyzed could also be a beneficial approach.

Exhibit 3-43. Sample Collection – 6-8 Cohort: All Sample Types

Part	Feb[1]	May[1]	Jun[2]	Jul[3]	Aug[1]	Sep[2]	Oct[3]	Nov[1]
019								
020								
021								
022								
023								
024								
025								
026								
027								

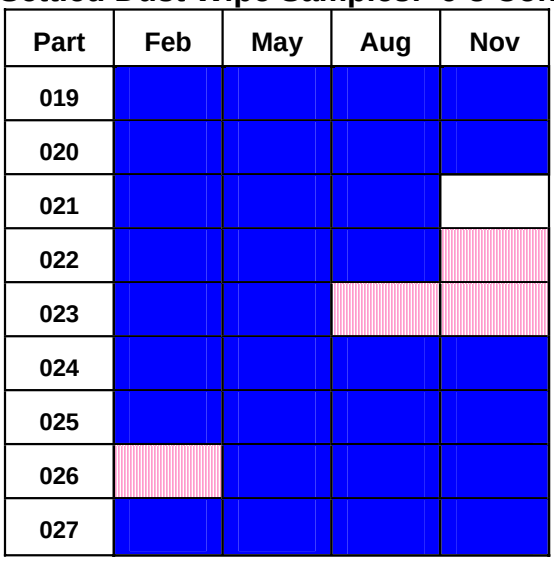
[1] Saliva and Dust Wipe Kit
[2] VOC Badge and HOBO Kit
[3] HOBO 42-Day Kit

Participant returned kit.

No kit returned.

Sample Collection Summary	
Total number of kits shipped	72
Total number of kits returned	70
Return sample rate	97% (70 returned kits/72 shipped kits)

Exhibit 3-44. Collection Summary and Condition Of Settled Dust Wipe Samples: 6-8 Cohort



Sample in acceptable condition for analysis. Acceptable sample defined as dust wipe appeared to contain dust and collection date recorded.

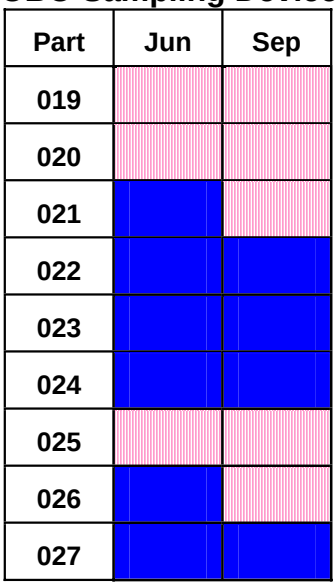
Sample in unacceptable condition. Unacceptable sample defined as either dust wipe did not appear to contain dust or collection date not recorded.

No sample collected

Sample Collection Summary	
Participant-months of dust wipe collection[1]	36
Dust wipe samples collected	97% (35/36)
Acceptable dust wipe samples collected	89% (31/35)

[1]Defined as the number of months when participants received materials to collect samples.

Exhibit 3-45. Collection Summary and Condition of VOC Badge/HOBO Sampling Devices: 6-8 Cohort



Sample in acceptable condition for analysis. Acceptable sample defined as cap was found on the VOC badge, secured with tape, badge packed correctly and collection date recorded.

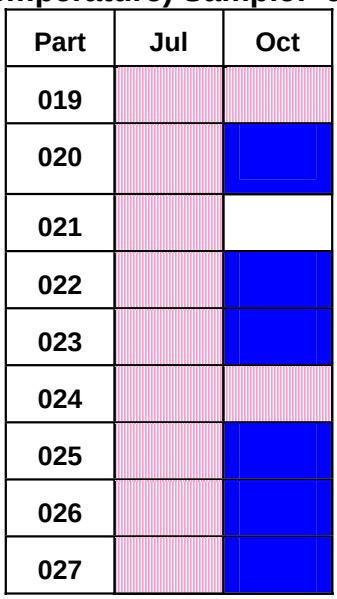
Sample in unacceptable condition. Unacceptable sample defined either cap was not found on the VOC badge, not secured with tape, badge not packed correctly or collection date not recorded.

No sample collected

Sample Collection Summary	
Participant-months of VOC badge collection[1]	18
VOC badge samples collected	100% (18/18)
Acceptable VOC badge samples collected	56% (10/18)

[1] Defined as the number of months when participants received materials to collect samples.

Exhibit 3-46. Collection Summary and Condition of HOBO (Temperature) Sample: 6-8 Cohort



Sample in acceptable condition for analysis. Acceptable sample defined as HOBO could be downloaded upon receipt, temperature was recorded correctly, samples collected for the entire 42-day period, and collection date recorded.

Sample in unacceptable condition. Unacceptable sample defined as either HOBO could not be downloaded upon receipt, temperature was not recorded correctly, samples not collected for the 42-day period, or collection date not recorded.

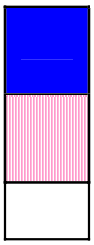
No sample collected

Sample Collection Summary	
Participant-months of HOBO collection[1]	18
HOBO samples collected	94% (17/18)
Acceptable HOBO samples collected	35% (6/17)

[1] Defined as the number of months when participants received materials to collect samples.

Exhibit 3-47. Collection Summary and Condition of Saliva Samples: 6-8 Cohort

Part	Feb	May	Aug	Nov
019				
020				
021				
022				
023				
024				
025				
026				
027				



Sample in acceptable condition for analysis. Acceptable sample defined as sample received cold, filled to the red line, contained no mouthwash, and collection date recorded.

Sample in unacceptable condition. Unacceptable sample defined as either sample not received cold, not filled to the red line, contained mouthwash, or collection date not recorded.

No sample collected

Sample Collection Summary	
Participant-months of saliva collection[1]	36
Saliva sample collected	97% (35/36)
Acceptable saliva samples collected	23% (8/35)

[1] Defined as the number of months when participants received materials to collect samples.

Acceptability of the VOC badge/HOBO samples was 56%, as shown in ***Exhibit 3-45***. This sampling procedure was problematic for several study subjects. Three of the participants never provided an acceptable sample, and two of the participants collected the sample properly the first time but not the second.

Selected VOC badges were extracted and analyzed. The VOC analysis data are shown in ***Appendix M-5***. The samples contained many of the target analytes except for *o*-dichlorobenzene. All of the sampled badges appeared to have been exposed for sample collection. There was variability among the concentrations measured and none of the samples indicated suspiciously-high VOC concentrations; this suggests that those samples that appeared to be collected properly were in fact collected properly. The blank samples showed small amounts of background for toluene and *p*-dichlorobenzene. Reproducibility of injections was very good, with percent differences between measurements ranging from 1 to 5%. However, the method recoveries were generally low, with most of the analytes showing approximately 40-50% recovery, with the exception of p-xylene, which showed a recovery of 88-99%. The reason for this is not clear but it is important to note that this does not in any way affect the conclusions of the study. The VOC analyses confirmed that samples considered acceptable based on visual inspection were probably handled correctly by the study participants.

The light intensities measured by the HOBOs with each VOC badge showed some compliance problems. As anticipated, light variations were substantial during the day while the badge was being worn and fairly small variations, if any, during the night time hours. From the June 18, 2002 shipment, the data suggested that four of the nine participants did not wear the badge for the entire 48 hours period, i.e., data looked as though the device was sitting on a shelf for prolonged periods when activity, and thus, light intensity variations, would have been anticipated. For the September 9, 2002 shipment, five of the nine participants did not wear the HOBO/badge combination for the required 48 hours. The HOBO's were pre-programmed to stop recording on September 26, 2002. Participants #21, 23, and 24 did not start the VOC data collection until after the HOBO had stopped recording data, thus no light data were available.

Finally, the acceptability of the 42-day HOBO data (i.e., data could be downloaded, temperatures recorded by the participant were in line with those recorded by the HOBO, data collected for full 42-day period, and the collection date was recorded) are shown in ***Exhibit 3-46***. Only 35% of the collected samples provided acceptable data. Acceptable samples were defined as those in which the data could be downloaded, temperature was manually recorded properly,

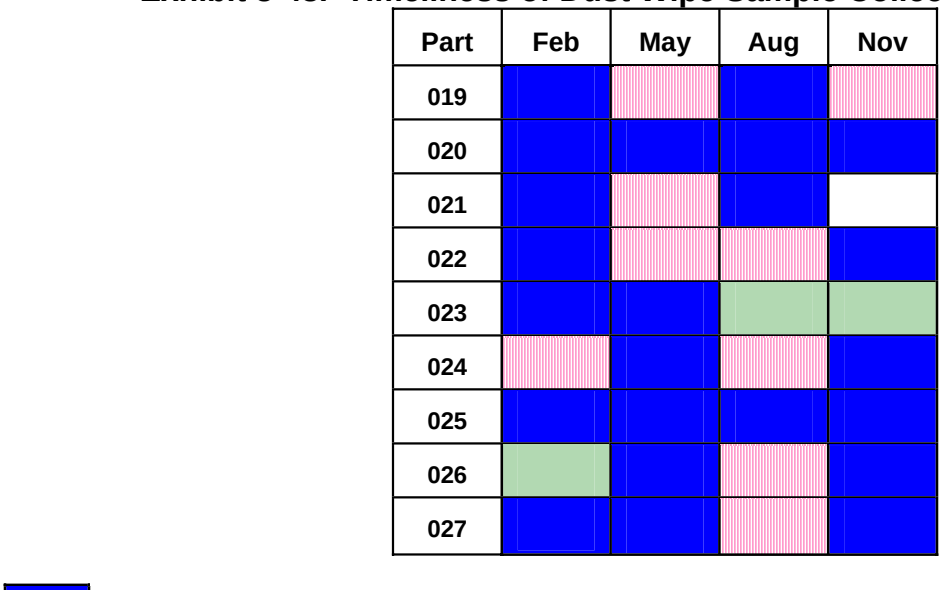
the sampling duration was 42 days, and the collection date was recorded. There were no participants that provided acceptable data for the July sampling; however six of eight that collected data in October provided acceptable data. A possible explanation for the unacceptable data collected during July was the timeliness with which study participants initiated sample collection. The impending need for the HOBOs to be shipped out for VOC sampling resulted in a request from KN to the participants that they return the HOBOs. If participants waited for several days before initiation of collection, they would have had to return the devices short of the requested collection duration of 42 days.

Timeliness. Data for dust wipes and saliva are shown in ***Exhibit 3-48 and 3-49***, respectively. We observed the same timeliness rates for dust wipes and saliva (66%). However, using a 7-day threshold for defining timeliness does not mean they were collected at the same time or on the same day. The variation in time between the collection of wipes and the collection of saliva was not investigated. Delays between the collection of an environmental sample and the corresponding biological sample can make studies difficult if the temporal linkage of samples is critical to success.

The data for timeliness of collection for the VOC badges are shown in ***Exhibit 3-50***. Only 50% of the samples were collected on time. However, given that this sample needed to be collected for a total of 48 hours, there was less flexibility in our threshold of 7 days for defining a timeliness collection compared to some of the other matrices. Any delay in starting collection following receipt of the package would make the deadline on the back end tighter.

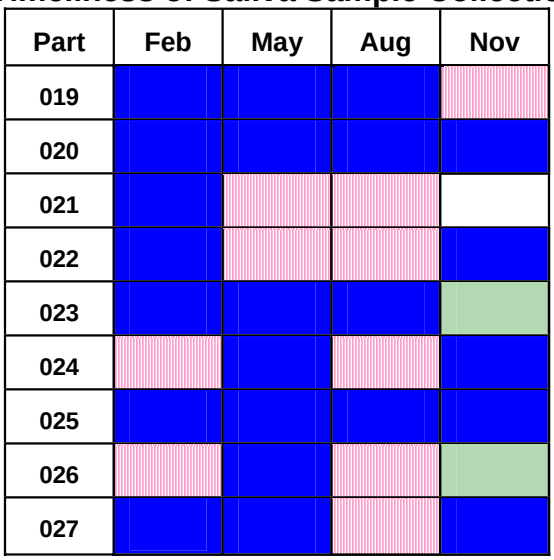
Finally, the timeliness data for the HOBO monitors alone is shown in ***Exhibit 3-51***. The number of samples promptly returned after 42 days was only 29%. Greater tardiness was observed in the second collection relative to the first collection. This could suggest fatigue with the study or that a sampling device that is left for a long period of time gets forgotten.

Exhibit 3-48. Timeliness of Dust Wipe Sample Collection: 6-8 Cohort



Sample Collection Summary	
Timeliness rate	66% (23 samples collected within 7 days/35 samples)

Exhibit 3-49. Timeliness of Saliva Sample Collection: 6-8 Cohort



Sample collected within 7 days of receipt of collection materials

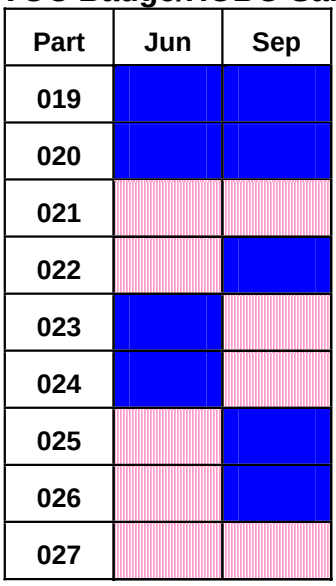
Sample collected after 7 days

Sample collection date not provided, but sample was collected

No samples collected

Sample Collection Summary	
Timeliness rate	66% (23 samples collected within 7 days/35 samples)

Exhibit 3-50. Timeliness of VOC Badge/HOBO Sample Collection: 6-8 Cohort



Sample collected within 7 days of receipt of collection materials

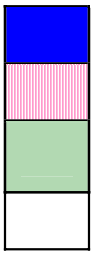
Sample collected after 7 days

No sample collected

Sample Collection Summary	
Timeliness rate	50% (9 samples collected within 7 days/18 samples)

Exhibit 3-51. Timeliness of HOBO (Temperature) Sample Collection: 6-8 Cohort

Part	Jul	Oct
019		
020		
021		
022		
023		
024		
025		
026		
027		



Sample collected and returned within 7 days of the 42-day collection period

Sample collected and returned after 7 days of the 42-day collection period

Sample collected and returned before the 42-day collection period was over. Date and temperature were not recorded on sampling log by study subject for the entire 42-day period

No sample collected

Sample Collection Summary	
Timeliness rate	29% (5 samples collected within 49 days/17 samples)

Compliance with instructions to date sample containers and complete metaquestionnaires after sampling was notable for the 6-8 cohort (***Exhibit 3-52)***. For all samples collected across all sample types, 100 (95%) had sample identification, and the collection date had been recorded. Of the 100 samples, non-compliance was most evident for the 42-day HOBO collection and was not surprising given the length of time associated with collecting this sample compared to other samples which typically involved a sample collection period of less than 48 hours.

For the 6-8 cohort, we saw that participants were not predisposed to collecting samples on any one day of the week (***Exhibit 3-53***), but generally there were more samples collected on weekdays than weekends. One notable observation was the VOC badge sampling, in which it appeared that many participants preferred to collect this 48-hour sample over the weekend.

3.3.6 Summary and Conclusions: 6-8 Cohort

Retention of participants in the 6-8 year old study was very good with eight of nine families continuing to provide data and samples in the last study month. However, recruiting study subjects was marginally successful in that only 31% of the eligible families agreed to participate. The one study subject not completing the study was from the low income strata.

Response rates for completing the metaquestionnaires (94%+) and providing samples (94%+) were very good (***Exhibit 3-54***). However, the samples collected by this cohort, notably saliva, VOCs, and HOBO temperature data collection, were in many instances unacceptable for analyses in the lab. Also, we noted that for many of the sample types, the samples were not collected in a timely manner (29% to 69% collected within the specified time period). Parents and children were very willing to provide saliva samples (97% response rate); however, few of the samples collected were acceptable for analysis (23%). These problems included no recorded collection date, sample contained mouthwash, or an insufficient collection volume. Alternative methods could be considered such as use of the salivette (pad that is chewed and absorbs saliva) or the approach of delaying the start of collection after mouthwash use. Selection of methods for future studies will depend upon the nature of the analysis, e.g., DNA from buccal cell, metabolites of organic compounds. If a certain volume is needed, investigators will need to request a larger volume than what is needed.

Exhibit 3-52. Temporality of Sample Collection and Metaquestionnaire Completion by Sample Type: 6-8 Cohort

Type of Sample	Total No. of Samples Collected	Samples Collected with Date Recorded (%)	Samples Meeting Temporality Requirement* (%)
Dust Wipe	35	91 (32/35)	91 (29/32)
Saliva	35	94 (33/35)	94 (31/33)
VOC/HOBO	18	100 (18/18)	89 (16/18)
HOBO (Temp)	17	100 (17/17)	82 (14/17)
Total	105	95 (100/105)	90 (90/100)

*Temporality requirement defined as sample was collected same day or day before metaquestionnaire was completed.

Exhibit 3-53. Samples Collected by Day of Week: 6-8 Cohort

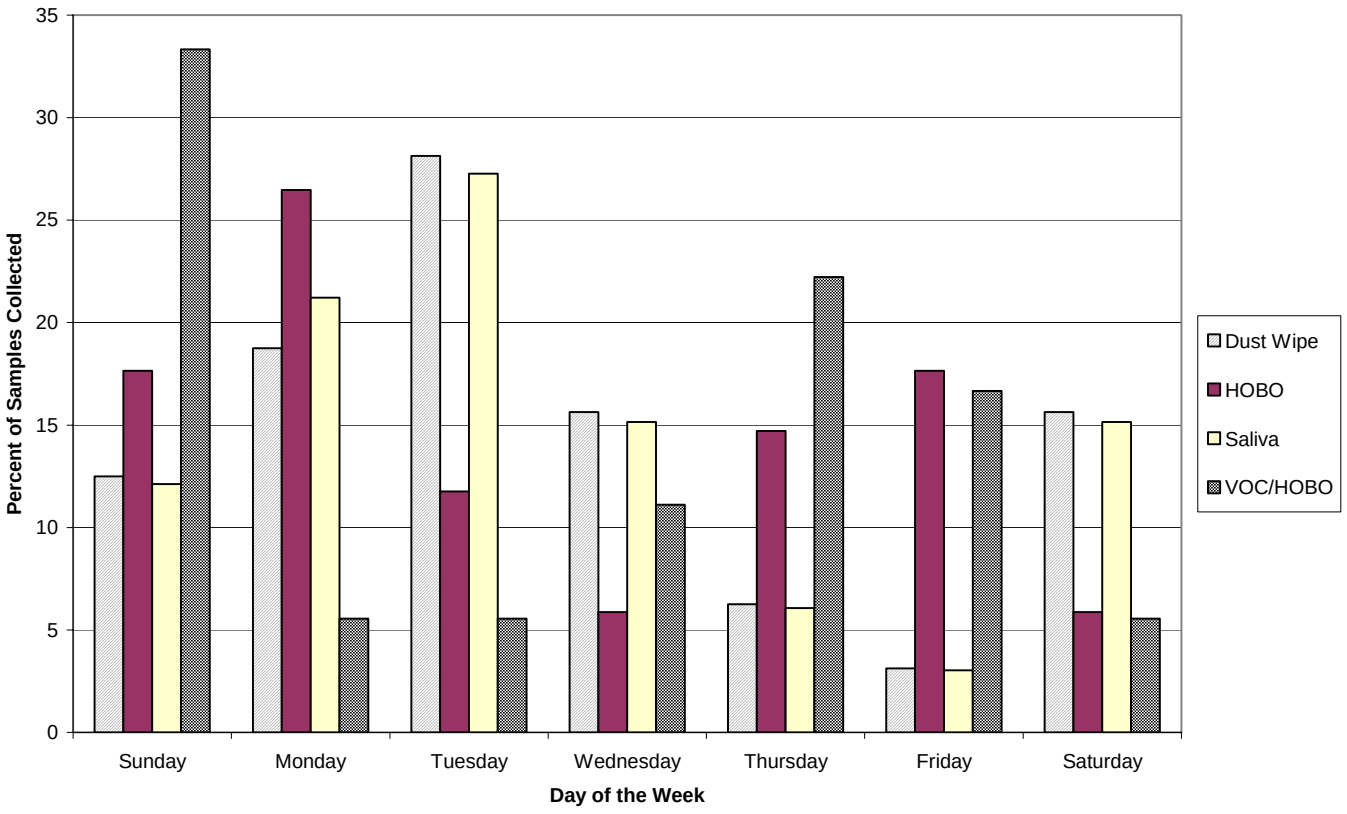


Exhibit 3-54. Summary of Data and Sample Collection: 6-8 Cohort

Sample/Data Collection	Percent Compl.[1]	Percent Accept.[2]	Percent with Acceptable Timeliness[3]	Percent with Date Recorded[4]	Percent with Acceptable Temporality[5]	Major Problems/Comments
Saliva	97	23	66	94	94	Large number of samples were unacceptable for analyses. Samples were received warm, had low volume, or contained mouthwash.
Dust Wipe	97	89	66	91	91	No significant problem.
VOC Badge with HOBO	100	56	50	100	89	Participants found VOC badge difficult to assemble. Many badges unacceptable for analyses. Some children did not like wearing the badge; concerns about peer acceptance. There were difficulties in downloading instructional video via WebTV.
HOBO (42-day)	94	35	29	100	82	Low number of HOBO sampling events with acceptable data.
MetaQx: Saliva & Dust	97					Participants had problems with a question about amount of time spent in various locations over 24-hour period.
MetaQx: VOC & HOBO	94					
MetaQx: HOBO	94					

[1] Percent Completed (Number of samples or questionnaires received ÷ total number of possible samples).

[2] Percent Acceptable (Number of samples considered to be acceptable for analyses ÷ total number of samples received). See exhibits and text for definitions of acceptability.

[3] Percent with Acceptable Timeliness (Number of samples received within 7 days of kit shipment ÷ total number of samples received).

[4] Percent with Date Recorded (Number of samples with date properly recorded ÷ total number of samples received).

[5] Percent with Acceptable Temporality (Number of samples collected same day or day before meta questionnaire completed ÷ total number of samples collected with date recorded).

[6] MetaQx (Metaquestionnaire)

Collection of dust wipe samples did not present many problems but some were considered unacceptable for analyses because of not noting the collection date or because very little dust was present. The use of an alternate method for settled dust, such as a dust plate that can integrate over a longer period of time could be helpful if the experimental design would allow for an integrated sample.

Even though the collection rate for VOC samples was 100%, use of the VOC sampling device was a problem for participants. Only 56% of the samples were acceptable for conducting analyses. The focus group participants also advised us that these samples would be difficult to collect because of assembling problems and acceptance by the child. We anticipated these problems and developed a video. Unfortunately, the video was not as accessible as we had intended. Even with limited access to the video and detailed instructions that were accessible to all via hardcopy and web, many participants could not effectively handle this sample type. The light intensity data suggested that that compliance was an issue. The data showed that one-half of the samples were not worn for the entire 48-hour period, and thus any conclusions based on the data would be suspect. Additionally, three of the participants were delinquent in starting the sampling activities during the second monitoring event.

The 42-day HOBO temperature collection was also not as successful as anticipated. This type of sample gave some problems that appear to be instrument-related as well as compliance-related. In one instance, the data could not be downloaded from the HOBO; return of the device to the manufacturer resulted in a successful download. Although only 35% of the collected samples were considered to be acceptable, the very low compliance rate for July was likely the result of a need to re-cycle the HOBOs for the VOC badge sampling effort. There was sufficient time for participants to complete the 42-day collection activity but not if they did not start for several days. As the time for shipment of the VOC badges approached, KN sent an e-mail to participants to request that they return the HOBOs. This could have caused folks not to sample for the requested duration. Some of the participants did not record the temperature manually using the schedule requested. A lack of manual recording would not likely impact data quality but served here as a measure of how well participants could comply with study demands. Parents said in the debriefing that the sample was not difficult to collect.

We also noted a problem with the metaquestionnaires for this cohort regarding questions in which respondents were required to account for time over a 24-hour period. There were instances in which the participants had difficulties in accounting for and summing time over a

24-hour period. Cognitive testing and modifications in the web-based study instrument should help to alleviate this kind of problem in future data collection efforts.

The burden placed on the study subjects was considered to be reasonable even though participants were asked to provide a variety of samples and metadata (***Exhibit 3-55***). Based on the debriefing data and the quality assurance visits and calls, we confirmed what we saw in the lab, that the VOC badge and saliva sample collection may have imposed a level of burden that was greater than that for the other samples.

Exhibit 3-55. Observations on Level of Burden: 6-8 Cohort

Sample/ Data Collection	Description of Activity	Duration[1] (min)	Level of Difficulty[2]	Participant Comments
Dust Wipe	Using the template and wet wipe provided, collect dust wipe sample. Record date and time on label. Store in freezer for until shipment. Package sample for shipment.	7	2	Participants noted it was not a problem to collect the dust sample or to place it in the special shipping container.
Saliva	Rinse mouth with mouthwash. Discard used mouthwash. Collect saliva in cup and fill to red line. Record date and time on label. Store in freezer until shipment. Package sample for shipment.	10	2	Four of the participants did not have a problem with collecting saliva from their child, whereas two reported it was a small problem.
VOC Badge	Watch instructional video. Remove VOC from can and attach screen guard. Wear for 48 hrs. Record dates and times. After 48 hrs, remove screen guard and separate sections of badge. Attach caps to open ends. Return to can for storage in freezer. Package sample for shipment.	12 (for assembling VOC badge)	5	One third said it was not a problem to assemble the badge and have their child wear it. One third said it was a small problem. One third said it was very difficult to assemble the VOC badges and obtain the cooperation of their child to wear it. There were problems in making the videos available to participants for viewing.
HOBO worn with VOC	Attach HOBO to shirt near VOC Badge. Wear for 48 hrs. Record dates and times. Return to plastic box for storage. Package sample for shipment.	5[3]	3	One child did not want to wear the HOBO while at camp because there were hobos nearby and was worried about being teased.
HOBO (Temp)	Remove HOBO from package and place on table or shelf. Place thermometer near HOBO. Twice per week record the date, time, and temperature for 6 weeks (42 days) on a data sheet. Package materials for shipment.	2 30[4]	2	Participants reported that it was not a problem to setup the HOBO or record the room and outdoor temperature.
MetaQx and Activity Diary	Questionnaire and activity diary are to be completed day after samples are collected using WebTV.	7	3	It was difficult to make duration of activities sum to 24 hours, potentially making Qx more cumbersome.

[1] Average duration of time to complete sample activity as reported by sample participant during debriefing; unless otherwise noted.

[2] RTI estimate of level of difficulty; Scale of 1 – 5, with 1 = easy and 5 = difficult.

[3] RTI estimate of duration

[4] RTI estimate of duration; participants may not have been taking into consideration the additional time to manually record data in the debriefing questionnaire.

4

Quality Assurance Procedures and Results

Quality assurance is a typical and integral part of exposure monitoring studies conducted and sponsored by US EPA. For these demonstration studies, a variety of QA activities were performed which included:

- developing and implementing a Quality Systems and Implementation Plan (QSIP) which included standard operating procedures (SOPs) (the QSIP and SOPs were submitted as a separate deliverable under the task order; the QSIP with its modifications received final approval on October 21, 2002);
- making calls and visits to participants to assess their compliance with procedures and discuss any problems that they had;
- communicating with RTI laboratory and project staff; and
- observing RTI activities.

4.1 Documentation

A QSIP was prepared at the outset of the task order, which detailed the quality assurance and quality control procedures for the study. The QSIP was revised when the laboratory analyses were added through a task order modification. SOPs describing RTI's activities were written and revised as needed. QA staff assisted with preparation of these documents and reviewed the final documents. QA staff also reviewed monthly progress reports to keep abreast of the overall project status.

4.2 Participant Follow-up

To follow up with participants, QA staff prepared a QA Audit Procedures guidance document that included questionnaire checklists and can be found in ***Appendix N*** for each cohort and received Institutional Review Board (IRB) approval before proceeding with contacting participants in late April 2002. The checklists covered the main points of the procedures that

participants were following. Calls and visits were generally scheduled approximately one week after sampling supplies were sent to participants. In addition to asking specific questions about the procedures, participants were asked to provide any comments that they had on the project and the procedures.

4.2.1 Visits

RTI staff visited two 3-5 cohort households in Ohio during July 2002, one 6-8 cohort household in North Carolina during May 2002, and one 0-1 cohort household in Illinois in December 2002. The same checklists ***(Appendix N)*** were used for both the visits and the calls, with a few additional items included for the visits.

4.2.2 Telephone Calls

RTI staff called to follow up with participants for 5% of the sampling events, for a total of 14 calls. The calls were spread over the period of the project and over the 3 cohorts – 5 for 0-1 cohort, 5 for 3-5 cohort, and 4 for 6-8 cohort. All sample types were covered with the telephone calls. The results of the calls and visits are summarized in ***Exhibits 4-1, 4-2 and 4-3***.

4.3 Laboratory Activities

QA staff observed RTI staff's shipping and receiving procedures during the second month of field data collection (March 2002) and confirmed that detailed records were maintained on outgoing and incoming shipments. QA staff also routinely reviewed weekly summaries and communicated with laboratory staff about any problems encountered. They also participated in some calls that laboratory staff made to follow up on problems with incoming shipments.

QA staff observed extraction of the VOC badges on January 6, 2003. Notes were made on problems found at the start of the extraction step, such as missing parts and loose lids. A written standard operating procedure (SOP) was followed for the extractions, and a separate SOP is available for analysis of the extracts by GC/MS.

4.4 QA Observations and Conclusions

The study approach minimized the level of human contact with participants, compared with what would normally be associated with this type of study when field technicians travel to the participants' homes. For the QA follow-up calls and visits, the participants were very

accommodating and seemed genuinely interested in performing the procedures properly. The calls and visits provided insight into the participants' experiences.

Even though the participants had RTI contact information, almost all had concerns and observations that had not motivated them to call us, but were brought to our attention during the QA interview. Many of the participants asked if they would be given the results of the research.

As ***Exhibits 4-1, 4-2, and 4-3*** indicate, a variety of topics were noted during the calls and visits. These may be broadly categorized as follows:

- Comments about logistics, such as shipping and Federal Express coordination and being prompted to complete the metaquestionnaire before they had time to collect the samples.
- Comments regarding procedures, convincing children to wear the monitors, accessing video instructions, completing surveys, assembling VOC badges, and using appropriate sock and diaper sizes.

Generally, the calls generated similar comments to the visits to the participants' home, but imposed less of a burden on the participants and were more cost effective. For a larger study, both calls and visits should be considered, but with the emphasis on calls.

Exhibit 4-1: Comments and Observations From Results of QA Visits and Calls: 0-1 Cohort

Participant No./ Date/Type of Sample	Comments and Observations
Part. 006 5/7/02 (C) Breast milk and urine	Participant asked about the point of the study and the payments for participating
Part. 009 6/7/02 (C) Duplicate diet and urine	Participant is at work when the packages are picked up. Participant tries to complete the questionnaire within 24 hours, but was a little behind this time. She had 2 sick children, but completed data collection within 48 hours. The sample kits usually come on Wednesday. The participant works outside the home and so generally collects the samples on the weekend. KN starts sending reminders too early, in her opinion, before she has had time to collect the samples. For the on-line survey question about when the diaper is put on and taken off, she consistently gets an error message about the times she enters being incorrect. She puts the diaper on in the evening (around 8 p.m.) and takes it off the next morning (around 6 a.m.). Participant tries to collect the same amount of food that the child has eaten, but it is sometimes hard to judge.
Part. 004 7/1/02 (C) Duplicate diet and urine	FedEx office in town so she drops the packages off. There was confusion one time with an old label. FedEx called thinking that they were shipping the package to her, not from her–so she now removes all old labels. The confusion delayed shipment when it occurred. This time, she was unable to get the metaquestionnaire to come up and e-mailed KN about the problem. Participant works nights several nights a week so she often has the samples in the freezer for more than one night.
Part. 005 8/26/02 (C) Duplicate diet and urine	Participant did not try to send the same volume of milk that her son drank, but did provide a sample of the whole milk that he was drinking.
Part. 008 12/17/02 (V) Duplicate diet and urine	The study subject reported that the sample collection has gone well and that she liked participating in the study. The hardest thing has been the time it takes to track everything, but that is not a problem. Nothing went wrong with the latest mailing and sample collection. She collected the duplicate diet sample on Saturday and the baby urine Sunday morning. She is not breast feeding. The samples were stored in her freezer. She had not mail them because she thought that the RTI QA specialist might want to see them. She was planning to mail them that week. For one of the sampling waves, only one diaper was sent, but she said that was not a problem. She found it easier to take the samples to the Fed Ex office near her office than to wait for pickup. Fed Ex was late twice in picking up. She said dropping the shipment off was not a problem. With regard to the WebTV, she thought they send too many reminders. Because she works, she can only do the sample collection on the weekend. She puts the diaper on the baby at night and takes the urine sample the next morning, she has had a small problem with the WebTV program, which assumes that the diaper is put on and the sample taken the same day. The program will tell her that the sample was collected before the diaper was put on. But all she has to do is hit ENTER.

Exhibit 4-1: Comments and Observations From Results of QA Visits and Calls: 0-1 Cohort (cont.)

Participant No./ Date/Type of Sample	Comments and Observations
Part. 001 12/28/02 (C) Duplicate diet and urine	She is no longer breast feeding. The participant said that she has sometimes had problems with error messages when she enters the times for the diaper on the questionnaire.

Exhibit 4-2: Comments and Observations From Results of QA Visits and Calls: 3-5 Cohort

Participant No./ Date/Type of Sample	Comments and Observations
Part. 015 4/22/02 (C) Socks and urine	Vacuum cleaner is water based and does not have a bag. Participant needed smaller socks for her child, and thought it would help to know the metaquestionnaire questions ahead of time.
Part. 017 4/23/02 (C) Vacuum bag and hair	Participant has a central vacuum system, which does not have a bag. She asked if notification about upcoming vacations is needed to coordinate schedules.
Part. 013 5/22/02 (C) Tap water	Participant turned off the water conditioner before collecting the sample. Participant did not observe a red line on the sample bottle that he used.
Part. 011 7/8/02 (V) Socks and urine	Participant has had trouble with the questionnaire at times. The child found the socks "itchy." The participant could not access the video instructions for the hair sample collection.
Part. 014 7/8/02 (V) Socks and urine	Participant had trouble with the questionnaire one time. The family replaced hardwood floors during one of the samples so there was probably extra dust. Participant wants to know if they will see the results of the study. Participant was unable to access the video instructions for the hair sample.
Part. 018 9/9/02 (C) Socks and urine	Participant noted that it is difficult to include the tape in the shipment back if she needs the tape to prepare the box for shipping. She pulls some strips of tape off to use to close the box before she puts the tape in the box. The socks were a little tight and not that stretchy.
Part. 012 12/3/02 (C) Tap water	Participant had received the box for socks and urine samples, but had not collected the samples yet. Participant does not check webTV electronic mail frequently. Child is stubborn about providing the urine sample. Participant asked about seeing the research findings.

Exhibit 4-3: Comments and Observations From Results of QA Visits and Calls: 6-8 Cohort

Participant No./ Date/Type of Sample	Comments and Observations
Part. 026 5/28/02 (V) Saliva and dust	Participant was not sure when to expect shipments. The box that the participant opened during the visit included a note asking that the participant return the dust template from last time, but she thinks she threw it away. The instructions did not clearly indicate that the template should be returned, she thought. She suggested adding the dust template to the checklist. There was an extra piece of paper or wipe in the plastic bag with the mouthwash and the sampling container this time. Was this supposed to be there? (It is to absorb any spills.) According to the instructions, the participant should e-mail KN to let them know that she is sending the package. The participant did not know an e-mail address for KN and thought that more specifics should be included about this. The participant was not sure how quickly the samples should be collected after she receives the sampling kit. (The instructions say that the samples should be collected within a week.) Since the last samples were collected, the road leading to the participant's home and the participant's driveway have been paved. They were gravel before. The house is less dusty now.
Part. 020 6/24/02 (C) HOBO and VOC badge	Earlier in the project, Federal Express left the packages at her house for her without a signature, but later Federal Express did not leave the packages if no one was home; she has now signed for them to always leave them; she takes the packages to work to ship back. Her son was concerned about being teased, especially with the name HOBO showing on the monitor–there are hobos near his day camp that the campers have been discussing. For the VOC badge, she was confused about which numbers to write where. Perhaps the instructions could be clarified. Some of the numbers were already written on the lid. The O-rings were black, not white as stated in the instructions. She had assumed that the samples would be the same as for previous months and did not open the box until Sunday. Her son was wearing the monitors the day of the call. They were beside his bed while he slept at night.
Part. 027 7/22/02 (C) HOBO and VOC badge	Participant had just returned from vacation and opened box, but had not started the 42-day HOBO sampling yet. Her child was not happy about wearing the monitors. She found wearing the monitors inconvenient, particularly during activities away from home. Her husband set up and packaged the monitors. They watched the video instructions.
Part. 025 10/16/02 (C) HOBO	The TV is currently out for repair and is expected back in about 2 weeks. Unable to access WebTV during this time. Participant asked about seeing the results of the study. The VOC badge was the most difficult of the measurements. She viewed the video instructions before she used it the first time. Participant had a period of trouble with viewing videos.

Exhibit 4-3: Comments and Observations From Results of QA Visits and Calls: 6-8 Cohort (cont.)

Participant No./ Date/Type of Sample	Comments and Observations
Part. 019 11/11/02 (C) HOBO	Participant had received the box for saliva and dust samples, but had not collected the samples yet. She asked if another check will be sent before Christmas. Federal Express leaves packages at her door if she is not home; she prefers that they leave them with a neighbor. The questionnaire is sometimes frustrating, because it will not accept certain numeric answers and, thus, she cannot always provide accurate information. She had viewed the video instructions for the VOC badge.

5

Recommendations

At the outset of the demonstration studies we posed several questions (***Section 1.0***) that we hoped would be answered by this project. In ***Section 5.1*** below, we provide short answers to these questions. ***Section 5.2*** summarizes our recommendations and suggestions for additional research.

5.1 Answers to Key Questions

Can study subjects be successfully recruited through a pre-existing web-enabled panel?

Yes. The web can be used successfully to recruit subjects. A very detailed recruiting e-mail/survey was critical in ensuring that potential subjects understood what was expected of them and why. Data from the debriefing surveys indicate that subjects felt informed and knowledgeable about the study requirements prior to hard copy informed consent.

Are the incentives used in the study appropriate for level of burden?

Possibly. We were able to ask this question of the 0-1 participants in the debriefing survey. Samples collected by this cohort included breast milk, duplicate diet and urine samples. Those data show mixed results, some said the incentive amounts for the 12-month study were appropriate, others said they were not.

Is the web a feasible way of collecting questionnaire, activity and food diary data?

Yes. The consistently high completion rates for web surveys, and activity and food diaries demonstrate that when survey burden is kept to a minimum, subjects will comply.

Can study participants coordinate the temporality requirements of collecting data shortly after biological and environmental samples have been collected?

Yes. Study participants were instructed to complete metaquestionnaires shortly after collecting the samples. Compliance rates were well over 90% across all sample types. In a few instances questionnaires appeared to have been completed before the sample was collected.

Can study subjects follow instructions and successfully assemble and/or use equipment for collecting samples of food and water, volatile organic compounds, urine, hair, breast milk and others?

Mostly, but some samples were easier to collect than others. Overall, we had relatively high collection rates for the biological and environmental samples that were collected. Some samples, such as hair, dust, and water were relatively easy to collect. Others, such as the VOC and saliva samples were difficult to collect correctly. Sample condition and acceptability was a problem with some sample types.

Can study subjects successfully receive supplies and ship samples?

Overall, yes. Study subjects were generally successful in receiving and shipping supplies. However, placing the burden of shipping on the study subject has its own set of logistical and technical issues. These include, for example, a greater number of communications between project staff and participants to discuss packaging problems and missing items; a potentially greater number of samples that have not been adequately cooled or packaged; or shipments that arrive at the laboratory on weekends and holidays even though instructions requested otherwise.

5.2 Recommendations

We made a number of observations while conducting the three demonstration studies. In general, the study demonstrated that a web-based approach to collecting data and samples from study subjects is feasible. We offer below several recommendations for additional research and suggestions for the NCS.

Study Planning

- The web is a feasible approach for collecting information that does not have to be collected in a clinical environment and for providing instructional and other information that includes graphics and images. This form of data collection, which should be considered for the NCS, is dependent upon the study subject having a television (and telephone in the case of the panel we used) or computer equipment. The web approach allows distribution of instructional materials in two forms—electronic and hardcopy, which may be beneficial to some families. Problems that we encountered with study subject access to videos can be addressed with new technologies. The QA interviews

indicated that in some instances the study subjects had computer-related difficulties with a particular question. These types of problems are not unusual and can be successfully addressed in a large-scale study.

- Cognitive interviewing and usability testing of the study instruments and instructional materials are needed for a large-scale study. Instances in which we asked participants to account for their activities over a 24-hour period and to sum time spent in various environments posed problems using the web-based approach.
- Consideration should be given to asking study participants, while they are completing questionnaires, about the level of burden being imposed on them by participating in the study. The information can be used to re-design data collection approaches, if they become necessary, in a long-term longitudinal study such as the NCS.
- To ensure an appropriate sample size of women who breast feed, it is important to consider over sampling this subgroup to maintain the requisite number of cases at the end of the study. It's also important to confirm breast feeding status at least two weeks prior to the start of the survey because it is difficult to predict loss of subjects who have ceased breast feeding.
- Planning activities need to ensure that activities requested of study participants are not affected by physical limitations, such as color blindness, etc. An example can be found in the pH data from tap water generated during this study. Although all possible causes for large differences between the pH values measured by participants and those measured at RTI have not been evaluated, an inability of a participant to distinguish shades of color on the pH test strips could have been a cause. It is recommended that proposed participant activities be evaluated with physical limitations in mind.
- There is a need to consider the effect of socioeconomic status (e.g., income level) on potential biases in data acquired to address specific hypotheses. Although the number of participants in this study was relatively small, there were indications that lower income participants were less compliant and had higher drop-out rates than those in higher income strata. Should a particular hypothesis need a study population from lower income strata, over-sampling will need to be considered to avoid biases in the resulting data.

Study Initiation

- Recruitment response rates for each of the three demonstration studies were relatively low. Each of the cohorts originated from a pre-existing panel that presumably had a favorable predisposition toward participating in surveys. Unlike phone and in-person surveys that give control to the interviewer to contact and recruit subjects, web recruitment delegates this control to the potential subject. Based on our experience, the recruitment period should allow at least four weeks per subject for the process to be completed. This process includes time for the potential subject to check their e-mail, respond to the recruitment invitation, receive via regular mail the hardcopy informed consent form, and mail it back.

Study Implementation

- Pre-notification and e-mail reminders proved to facilitate compliance and timely completion of the web surveys, and the activity and food diary in a low cost and efficient manner. Subjects were expected to complete the survey requirements (web survey or diary and sample collection) within one week of receipt of the sampling materials. As a result, e-mail reminders were sent after Day 3 for all subjects and after Day 7 for non-respondents. Future longitudinal surveys that use the web may want to tailor the frequency of the e-mail reminders to the needs and habits of the household. Some study subjects voiced complaints about the frequency of the e-mail reminders and noted that they did not think it was necessary.
- We demonstrated that timely shipments to participants are possible. However, return shipments were more problematic. There were numerous instances in each of the cohort studies in which supplies, like the breast pump, were not returned and staff needed to follow up. The expense associated with staff communications with study participants needs to be factored into future studies of a similar nature. Another important consideration is the fact that participants sometimes ignored requests to *not* ship samples for Saturday or holiday delivery. Careful attention needs to be paid to this aspect of study implementation so that samples are in good condition when received. Procrastination in the collection of and return of samples was also a problem in some cases. The consequences on shipping equipment for subsequent sample collection events

can be problematic, especially in large studies with limited equipment. It might be worth considering a decrease in the incentive for very late samples.

- Additional testing of samples that are collected in a liquid state but are required to be shipped frozen or cool is warranted. We observed instances in the 0-1 cohort, for example, in which samples were leaking or warm when they were received. Given the variability that may exist in participants' homes for preparing, storing, and shipping samples, increased cooling capacity during shipping and longer freezing times are among the items needing to be investigated to ensure that samples are suitable for analyses when they are received.
- Tap water was relatively easy to collect in the 6-8 cohort study. However, we used a straight forward and simple protocol that might not be adequate for the full range of analyses needed for the NCS. Should preservatives be needed, e.g., thiosulfate or acid, additional thought needs to be given to how this can be accomplished without compromising participant safety. For the collection of water for the analysis of organic compounds of low volatility, thiosulfate and a solid buffer could be added at the time of collection, or even be placed in the bottle itself beforehand to optimize conditions for the target analyte. Extra care will be needed to explain the safety concerns to participants. In some cases, the risk might be deemed unacceptable. Alternatively, water could be acidified upon receipt at the lab if stability over a 2-day shipping period is not a major consideration. The sampling approach will obviously depend upon the purpose of the sample. Shipping sample collection containers with additives should not be a concern given the low toxicities. Leakage of sample containers should be addressed.
- Use of the VOC sampling device was difficult for participants. Improved instructional materials might improve the acceptability of samples arriving at the lab. However, the situation observed in the 6-8 cohort might indicate that such devices cannot be used when a high rate of acceptability is needed. This might also argue for a much more passive approach such as monitoring based on sensors or some other means that does not require the participant to do much. Additional research into an appropriate method for measuring VOCs is warranted.
- The feasibility of using less rugged instruments/devices should be evaluated as appropriate. For example, an aerosol nephelometer is a device used to measure real-time particle concentrations and is a candidate for use should particles be the focus of a

specific hypothesis. This instrument is somewhat fragile and requires set-up. In such cases participants would need to set up the device and take special care in packaging the device for return shipment. Given that participants in the current demonstration study had difficulty following assembly and packaging instructions, more complex and fragile devices could be problematic.

- Even though the purpose of these demonstration studies was to evaluate the feasibility of having study participants collect biological and environmental samples, we need to consider the use of technicians to aid in the collection of important, yet difficult, samples to maximize the number of such samples that are acceptable for laboratory analysis. Less expensive collection approaches for important samples is of no value if the resulting data are unreliable.
- We should also evaluate further the ability of study participants to comply with temporality of environmental and biological samples. This factor will be very important if a specific, time-dependent linkage is requested to evaluate a biological marker following an environmental exposure. That is, temporal linkages can be critical, depending on the hypothesis being tested, and it is important to understand anticipated compliance and its effect of the value of the resulting data.

Each of the demonstration studies collected more information than could be analyzed for this task order. Additional analyses of the information collected in the metaquestionnaires, such as the extent to which study subjects in the 3-5 cohort successfully responded to the questions about pesticide use, may be worthwhile. The chemical analyses samples that we performed were conducted primarily for purposes of assessing compliance and to confirm that study subjects had collected the samples as requested (e.g., creatinine in urine). Many of the samples were not analyzed and further research may be appropriate including looking at associations between demographic factors or responses on the metaquestionnaires and the levels of toxic substances in the samples. Using the web in the NCS is a worthwhile consideration and may be appropriate for data collection and study communications with the public, health care community, and study participants. For these demonstration studies, we used an existing panel as a source of study subjects. The NCS participants could be considered a special panel that would require establishing links and processes for transmitting information. Additional research may be appropriate to investigate the logistical aspects of implementing web-based data collection in the NCS.