Title:

Rapid Acquisition of Pre- and Post-Incident Disaster Data Study

Short Title:

RAPIDD Study

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Sponsored by:

National Institute of Environmental Health Sciences (NIEHS)

Principal Investigator:

Stavros Garantziotis, MD

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List of Abbreviations

AE	Adverse event
ASPR	Assistant Secretary for Preparedness and Response
BMI	Body mass index
BRFSS	Behavioral Risk Factor Surveillance System
CDC	Centers for Disease Control and Prevention
CDS	Clinical Data System
CFR	Code of Federal Regulations
cm	Centimeters
CPL	Central processing laboratory
CRF	Case report form
CTDB	Clinical Trials Database
DERT	Division of Extramural Research & Training
DHHS	Department of Health and Human Services
DMIS	Disaster Medical Information Suite
DMS	Data Management System
DNA	Deoxyribonucleic acid
DR2	Disaster Research Response Project
DTA	Data Transfer Agreement
eCRF	Electronic case report form
EOC	Emergency Operations Center
EDTA	Ethylene diamine tetraacetic acid
EPA	Environmental Protection Agency
EPL	Environmental Pathology Laboratories
ERHMS	Emergency Responder Health Monitoring and Surveillance
ESF #8	Emergency Support Function #8 (Public Health and Medical Services of the National Response Framework)
FOG	Field Operations Guide
FVC	Forced vital capacity
HRSA	Health Resources and Services Administration
ICF	Informed consent form

IRB	Institutional review board
kg	Kilograms
mmHg	Millimeter of mercury
mRNA	Messenger ribonucleic acid
MTA	Material transfer agreement
NBSB	National Biodefense Science Board
NDMS	National Disaster Medical System
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Heath
NIOSH	National Institute for Occupational Safety and Health
OHRP	Office of Human Research Protection
OHSR	Office of Human Subjects Research
PD	Protocol Deviation
PI	Principal Investigator
PII	Personally identifiable information
QC	Quality control
RAPIDD	Rapid Acquisition of Pre- and Post-Incident Disaster Data (Study)
RNA	Ribonucleic acid
SAE	Serious adverse event
SAMHSA	Substance Abuse and Mental Health Services Administration
SSS	Social & Scientific Systems, Inc.
UP	Unanticipated Problem
VPN	Virtual private network
WETB	Worker Education and Training Branch
WTP	Worker Training Program

Protocol Summary

Full Title:	Rapid Acquisition of Pre- and Post-Incident Disaster Data Study
Short Title:	RAPIDD Study
Conducted by:	National Institute of Environmental Health Sciences
Principal Investigator:	Stavros Garantziotis, MD
Primary Objective	To create a research registry comprised of disaster response workers who are rostered before or immediately after deployment to a disaster area
Secondary Objectives:	• To gather sociodemographic, health status, occupational exposure, and lifestyle information of the cohort before or immediately after deployment to a disaster area • To collect, process and store biological samples to allow estimations of disaster-related exposures of the disaster response worker cohort before or immediately after deployment to a disaster area • To establish a well-characterized disaster response worker cohort that will allow for future analyses of associations between disaster exposures and health outcomes
Study Design:	Registry study
Study Population:	The study population will include disaster responders who are deployed to a disaster area to conduct emergency response activities.
Accrual Duration:	The accrual duration will depend on the nature of the disaster that becomes the focus of this research project. The accrual of participants will begin early in the disaster response phase and will end when the targeted sample size is reached.
Registry Duration:	Participants will be enrolled in the study for follow-up by researchers for 10 years or longer, depending on the size of the registry, what we learn from future analyses, and/or the scientific or public health necessity.
Sample Size:	The sample size will depend on the prevalence of exposures and outcomes of interest for the disaster under study. We will use sample size estimates for a range of exposure and disease prevalence scenarios to guide our enrollment target.
Endpoints:	The study is designed to allow for the investigation of a wide range of outcomes of interest for a given disaster scenario.

Précis

Disasters are frequently associated with environmental exposures and socioeconomic disruptions that may lead to short- and long-term health consequences. Disaster response workers are potentially at the greatest risk for adverse outcomes due to direct exposure to hazardous environmental contaminants during the emergency response process. The importance of conducting disaster responder research in the immediate aftermath of disasters has become widely recognized, but numerous barriers to doing so have also been recognized. The Rapid Acquisition of Pre- and Post-Incident Disaster Data (RAPIDD) protocol aims to address this gap by registering and characterizing a cohort of disaster response workers early in the disaster response phase to obtain baseline characteristics. Disaster response workers deployed to a disaster area to conduct emergency response activities will be targeted for enrollment. Disaster responders may include police, fire, and emergency medical personnel, as well as other responder groups such as public health personnel and workers involved in environmental remediation and restoration activities. The primary objective of the RAPIDD study is to create a research registry comprised of disaster response workers who are rostered before or immediately after deployment to a disaster area. Important secondary aims are to administer questionnaires and collect biological samples to characterize the cohort in a manner that will allow for future prospective analyses of associations between disaster exposures and health outcomes. In order to achieve these aims, we have developed a protocol, operational manuals, questionnaires, data collection systems, training plans, and other tools to reduce the time required to initiate disaster research. We will also obtain scientific and regulatory approval of the protocol in advance of the disaster in hopes that expedited amendments, with clarifications of the research, will minimize delays associated with various review cycles.

In order to characterize the cohort prior to their involvement with response activities that could lead to disaster-related exposures, we will attempt to collect a wide range of questionnaire data, clinical measurements and biological samples. Questionnaires may cover topics including contact information, demographics, socioeconomic status, medical history, current physical and mental health status, occupational exposures, alcohol and tobacco use and other lifestyle factors.

Biological specimens collected may include the following: blood, urine, nail clippings, saliva, buccal cells or hair. Clinical measurements may include vital signs, anthropometric measurements and spirometry. By seeking IRB and other regulatory approvals for carrying out this research in advance, we anticipate that we will be able to submit expedited amendments to clarify the research plan for a specific disaster so that research can be initiated early in the response phase. However, in the very early phases of some disaster situations, it may not be safe or feasible to collect the data needed to fully characterize a cohort of response workers. In these situations, data collection may be limited to rostering and limited self-collection of biospecimens. As the response effort stabilizes and more becomes known about potential exposures and related adverse health outcomes,

we intend to expand our data collection effort, and we will seek expedited regulatory approval to do so.

1 Key Roles

For questions regarding this protocol, contact Stavros Garantziotis, MD (see contact information below).

Institutions:

Institution	**NIEHS, National Institutes of Health (NIH)**
Address	Clinical Research Unit, Bldg. 109, Rm. 109 111 TW Alexander Dr. Research Triangle Park, NC 27709-0002
FWA#	00005897
Contact Person	**Stavros Garantziotis, MD**
Phone Number	919-541-9859
Fax Number	919-541-9854
E-mail Address	garantziotis@niehs.nih.gov

Investigators:

Principal Investigator:	**Stavros Garantziotis, MD** Principal Investigator, Clinical Research Program National Institute of Environmental Health Sciences Clinical Research Unit, Bldg. 109, Rm. 109 111 TW Alexander Dr. Research Triangle Park, NC 27709-0002 Phone: 919-541-9859 Fax: 919-541-9854 E-mail: garantziotis@niehs.nih.gov

2 Background Information and Scientific Rationale

2.1 Background Information

2.1.1 Call for Scientific Investigations Following a Disaster

Following recent natural and man-made disasters, the importance of incorporating health-related scientific investigations into disaster responses has become widely recognized. The far reaching environmental health impacts of Hurricane Katrina in 2005, the Deepwater Horizon (DWH) oil spill in 2010 and the 2011 Tohoku earthquake in Japan, with its subsequent tsunami and nuclear

reactor incident, all underscore the need for research to illuminate the short and long-term impacts of disaster. In a call to action published in the New England Journal of Medicine in 2013, the Assistant Secretary of Preparedness and Response (ASPR) and the heads of NIH and CDC wrote that "the knowledge that is generated through well-designed, effectively executed research in anticipation of, in the midst of, and after an emergency is critical to our future capacity to better achieve the overarching goals of preparedness and response (1)."

Yet, barriers to conducting timely research remain. Following the 2009 H1N1 pandemic, the safety and efficacy of an unapproved antiviral, peramivir, remained unclear despite its being widely administered under an FDA emergency use authorization (2). While there was broad interest in rapidly setting up clinical trials, the difficulty of obtaining IRB approvals at each of the hospital institutions in which it was used and other obstacles proved insurmountable resulting in a missed scientific opportunity. Gaps in timely disaster responder research persist as well, despite the recognition of the unique risks associated with occupational exposure to disaster-related hazards. The DWH oil spill revealed a lack of adequate public health information about the environmental and occupational health risks of oil and dispersants (3). While longitudinal studies of exposed workers eventually were put in place, data collection did not begin until almost a year after the spill (1). These delays in research are harmful not only because they hold up the discovery of new findings but because they result in the loss of perishable data that is difficult to reconstruct months or years after the event. A key issue commonly encountered in optimizing disaster planning and response is how to collect credible baseline information in a consistent and timely manner. Collection of baseline information at the onset of a disaster would improve decision-making during and after the incident and also help clarify the short- and long-term health impacts of the event. New approaches to disaster research are needed to facilitate rapid collection of before and during the early phases of disasters.

2.1.2 Available Resources and Limitations

A 2011 report from the National Biodefense Science Board (NBSB) highlighted the capabilities and resources at the federal level that could be involved in the collection of disaster data. The report also suggested the cataloguing of currently existing data sets, which might be used to provide baseline information for certain scientific investigations, such as the National Health and Nutrition Examination Survey (NHANES) and Behavioral Risk Factor Surveillance System (BRFSS) (4). While NHANES and BRFSS can be useful as a source of baseline data, they each have significant limitations for use in a disaster when it may be unclear what baseline data is of critical importance and when areas of research interest may not be addressed in either survey. Furthermore, these systems provide only secondary general population data and may shed little light on unique segments of the population such as disaster response workers. These shortcomings highlight the need for the initiation of rapid primary data collection in the midst of an emergency.

Currently, there are a limited number of rapid assessment and research toolkits readily available and in use. Those that are available are somewhat restricted in the information they provide and in the timeliness and coordination with which they can deliver that information. One notable data gathering effort that has achieved some degree of success is the Disaster Medical Information Suite (DMIS), which has been created within the National Disaster Medical System (NDMS). DMIS combines three components: an electronic health record created for use in the field and for patient evaluation; a patient-tracking tool to follow injured or ill disaster victims; and a web-accessible Health Information Repository that can be used for surveillance in real-time and analysis of injuries and illnesses that are reported (4). While the DMIS is particular useful for short-term situational public health reporting, it was not designed for use in research studies.

A resource that is particularly salient for the collection of health data from disaster workers is the Emergency Responder Health Monitoring and Surveillance (ERHMS) system. The ERHMS system was developed by CDC's National Institute of Occupational Safety and Health (NIOSH) in coordination with the US National Response Team (NRT) and other stakeholder agencies. The *NRT Technical Document* provides guidelines and recommendations for the ERHMS system and data collection tools for the pre-deployment, deployment and post-deployment phases of a disaster response and recovery. While ERHMS addresses a key disaster worker data collection gap, the focus of its framework is primarily on improving public health practice and not informing disaster worker research.

Despite these evolving resources, the NBSB report concludes that additional infrastructure is needed in order to rapidly collect, analyze, and report detailed clinical data early in a disaster.

2.1.3 NIH Response and Resources

The NIH has a rich history of responding to disasters, particularly through NIEHS involvement in disasters with environmental components. Over the last decade, NIEHS has responded to broad range of disasters including Hurricane Katrina, the 2009 H1N1 pandemic and, most recently, the 2014 Elk River chemical spill in West Virginia. Notably, NIEHS is conducting the largest study of the long-term health impacts of the 2010 DWH Oil Spill on workers and volunteers who were involved in clean-up activities. The NIEHS also hosts the Worker Education and Training Branch (WETB) which administers the Worker Training Program (WTP) and delivers high-quality training to workers who are involved in handling hazardous waste or in responding to emergency releases of hazardous materials.

In response to recent disasters and the need for scientific investigations, the NIH has committed to fund The NIH Disaster Research Response (DR2) Project. The DR2 project aims to create a disaster research system consisting of a disaster research protocol that can be rapidly implemented, along with pre-established data collection instruments, equipment, materials and manuals for

collecting biological samples and clinical data, training materials, and a pre-identified team to carry out the research. This proposed study will help fulfill this project goal by conducting a research study with resources that will be identified and developed in advance of the disaster under study.

2.2 Rationale

The barriers to conducting disaster research during an active event must be addressed in order to accomplish the goals of preventing and reducing injury, illness, disability, death, and damage, while also bolstering recovery efforts and our understanding of health effects associated with an assortment of disasters. Although advances have been made in the area of disaster research over time, there is still a need for better designed and more effectively executed research strategies that can address the challenges to conducting disaster-related research (1), particularly during the early stages of an event.

Several key areas can be addressed in order to achieve more timely research responses to natural and man-made disasters (5). These include access to funding, expedited institutional review board (IRB), scientific review and Office of Management and Budget (OMB) approval processes, methodology standardization, development of pre-approved protocols that can be implemented immediately, and having operations and supplies in place to initiate the rapid collection of baseline information. The RAPIDD Study has been developed to address many of these issues and to demonstrate the feasibility of consistent and rapid collection of time-critical samples and data during a disaster scenario.

Scientific investigations during a disaster response can either seek to provide shorter-term findings to guide decision making during the response phase or to provide the foundation for studying longer-term exposures and potential health effects (4). In either case, successful implementation of RAPIDD has the potential to provide valuable, timely information such that future research is not limited due to a lack of adequate baseline information.

2.3 Discussion of the Protocol Structure

In their 2011 report, the NBSB offers a list of recommendations for improved mobilization of scientific resources in the investigative response to disasters that threaten public health, which includes developing “the concepts, doctrine, infrastructure, and personnel needed to begin scientific investigation and data collection rapidly in various types of incidents” (4). Implicit in this NBSB recommendation are two key principles: First, responses should be rapid. Second, variation in the responses should be addressed during the planning process.

The RAPIDD protocol was structured with those two key principles in mind.

We are seeking approval for a protocol that allows for a range of data collection activities early in the response phase of a future disaster. We intend to submit an expedited amendment to clarify the disaster setting, target sample size,

exposures and potential health effects of interest, specific questionnaires and procedures that will be implemented. This approach will reduce the time between IRB and study initiation by completing the full protocol prior to the disaster event. A Protocol Amendment Checklist (Appendix B: Protocol Amendment Checklist) has been developed to streamline this process and to allow an expedited review of the protocol.

A number of elements of the study are expected to remain the same, regardless of the disaster in which the protocol is implemented. Study elements that are expected to remain unchanged (e.g., descriptions of the procedures performed, risks of procedures, and human subjects protection measures), have been placed in the main body of the protocol. In contrast, some aspects of the protocol cannot be specified in advance, such as the disaster setting and target sample size.

2.4 Integration of Research with Other Agencies

It is anticipated that this research will be conducted as part of an overall response effort with multiple agencies involved in disaster-related operations. The delegation of authority for these activities are described under the disaster declaration process in the Stafford Act which requires an official request to FEMA for federal disaster assistance from the Governor of an affected State (i.e., activation of research assets will only occur by invitation of the affected community). Typically, a local emergency operations center (EOC) is designated as the central hub for coordinating all disaster response activities. Local, state and federal agencies represented at the EOC provide situational data through the chain of command using the Incident Command System. Through the integration of disaster research activities into ESF-8 (Emergency Support Function) activities of the National Response Framework (a goal of the NIH DR2 project), the RAPIDD study team will have authorization for operational conduct and access to knowledge about the disaster and possible health impacts. For example, the Environmental Protection Agency (EPA) and the CDC National Institute for Occupational Safety and Health (NIOSH) have experience and specific expertise in the collection of environmental samples to measure possible exposures to toxic substances after disasters. The RAPIDD Study will not duplicate the activities of these experts; rather the study team will seek to obtain the environmental sampling data from these agencies (via integration into ESF-8) and develop linkages with exposure data collected from the study cohort. While DR2 is a program of federal disaster research assets it may be integrated with research entities (e.g., academic institutions) within the local community. It is fundamental to the success of research activities for DR2 to conduct scientific investigations that fulfill the needs of the local community. Community engagement efforts are further discussed in Section 2.5.

2.5 Community Engagement and Pilot Activities

The goal of community engagement activities is to obtain buy-in for RAPIDD from disaster responders and engage the responder community in study design,

implementation and evaluation. Close and ongoing community engagement is expected to enhance the scientific validity of the study, make it more broadly relevant from a public health perspective, and expand its benefits to the affected communities. Community engagement activities will take place in the pre-approval phase and will continue throughout the implementation phase of the study to assure that the RAPIDD study reflects the interests of the selected disaster responder study cohort. One community engagement strategy that has been utilized successfully is to simulate the activation and implementation of the RAPIDD protocol in a disaster scenario tabletop exercise. These exercises provide the opportunity to notionally pilot-test RAPIDD recruitment, consenting and study procedures and obtain real-time feedback from representatives of the target cohort.

The initial pilot test of the RAPIDD protocol was held in Houston, Texas in February 2015. During the Houston pilot test, prospective disaster responders from the fields of public health, emergency management and first responder agencies were queried about their likelihood of participation in a RAPIDD study after receiving simulated recruitment messages and reviewing informed consent materials. Input from disaster responders and public health practitioners gave the RAPIDD study team a better understanding of the barriers to recruitment and enrollment and provided ideas for community-based strategies to address these barriers. This initial pilot also allowed us to better tailor messages to potential participants about the study's purpose and importance. Based on the feedback from the Houston pilot, we are encouraged that the protocol is functional. However, additional pilot testing is necessary to assure that the broader disaster responder community has ample opportunity to place their stamp on any proposed responder research, such as RAPIDD, that will play such a significant role in improving our understanding of the health and safety of workers engaged in disaster response.

We intend to conduct additional pilot tests of the RAPIDD protocol at other venues in order to assure that the prospective cohort's interests are fully addressed. Using a mix of focus groups, informant interviews and interactive tabletop exercise sessions, we plan to solicit feedback from additional representatives from the disaster responder community at local, state and national conferences. The RAPIDD study team has established contacts with the Worker Education Training Branch (WETB) at NIEHS which supports the training and education of workers engaged in activities related to hazardous materials and waste generation, removal, containment, transportation, and emergency response. The WETB holds biannual awardee meetings which may be a target for future pilot activities. These pilot activities will provide the RAPIDD study team with valuable experience in implementing the study and will help identify any potential operational constraints or optimizations needed in the overall design.

Community engagement activities will not be limited to the pre-implementation phase but will continue during implementation and through results dissemination to assure that the study is reflective of the needs of the local community. Similar

to community engagement efforts conducted for the NIEHS GuLF study, the RAPIDD study team will establish contacts with representative worker organizations, worker unions and other worker advocacy groups to identify the primary issues of concern locally and to discuss study implementation issues. A community advisory group (further discussed in Section 2.5.1) will be established to coordinate a systematic approach to obtaining continuous feedback from the targeted cohort.

2.5.1 Disaster Responder Community Advisory Group

After disaster strikes, a Community Advisory Group will be created to provide continued advice on the study and outreach efforts. The group will consist of up to 15 members representing local communities, organizations representing worker groups, as well as various occupational groups and is expected to engage in the following activities:

- Facilitate dialogue between disaster responder community members and the study team
- Identify effective communication strategies and vehicles tailored to the disaster responder communities' needs
- Assist in the dissemination of study related information locally and regionally
- Host disaster responder community meetings
- Proactively identify issues of concern with study implementation and options for resolutions
- Retain participants in the registry over time

A Community Advisory Group chair will be carefully selected from among its members and will work in close collaboration with the study investigators. The Community Advisory Group will meet regularly throughout the entire study duration.

2.6 Example Implementation of this Protocol

To help illustrate how this protocol will be executed, an example is described in Appendix D: Examples of Protocol Implementation During a Disaster Scenario of the actions the study team would take to implement the protocol under the described disaster scenario. While a hurricane scenario is used to describe a possible use of this protocol, the RAPIDD protocol is intended to be adaptable for use in any disaster of research interest.

3 Study Objectives

3.1 Primary Objective

The primary objective is to create a research registry comprised of disaster response workers who are rostered before or immediately after deployment to a disaster area.

3.2 Secondary Objectives

Secondary objectives are:

- To gather sociodemographic, health status, occupational exposure, and lifestyle information of the cohort before or immediately after deployment to a disaster area
- To collect, process and store biological samples to allow estimations of disaster-related exposures of the disaster response worker cohort before or immediately after deployment to a disaster area
- To establish a well-characterized disaster response worker cohort that will allow for future analyses of associations between disaster exposures and health outcomes

4 Study Design

4.1 Description of the Study Design

This is a registry study conducted to establish and characterize a cohort of disaster responders deployed to a disaster area to conduct emergency response activities. The registry data and samples will be available for use in future scientific investigations, which will require additional scientific and ethical reviews.

4.1.1 Recruitment

In most cases, it is anticipated that recruitment will primarily occur in a group setting adjacent to the disaster site (e.g., disaster worker staging area). There may also be situations when groups of potential participants are pre-identified (e.g., from a roster of disaster responders obtained prior to their deployment); in this case attempts to contact possible cohorts of interest to promote study enrollment may be made.

If feasible, the study may be advertised and potential participants may be contacted through various mechanisms (e.g., email, phone, flyer, text message, approached at a disaster site or training session) as part of an overall study recruitment strategy. Recruitment strategies will be sensitive to the fact that

disaster responders are engaged in critical emergency operations that may be prioritized over research considerations.

All of the methods used to recruit participants would provide an overview of the study and ascertain participant interest. The RAPIDD team will develop study brochures and FAQs (Frequently Asked Questions) that can quickly inform prospective participants of study aims. Interested individuals who are a part of a cohort of interest may be asked to provide contact information as part of the recruitment process so that they may be contacted and provided with further information for attending a registry visit at the work site (see Section 4.1.2).

Study documents and recruitment materials are currently developed in English, but speakers of other languages may be included depending on the disaster responder community involved. Translated materials will be developed for these populations and submitted as an amendment to the IRB for approval. Effective strategies for the development of culturally appropriate recruitment materials for the study cohort will be determined by soliciting participation and input from representatives of the target cohort. Bilingual study staff will work with non-English speaking individuals to the extent possible for anticipated languages (e.g., Spanish). The study team may also use telephone or video remote interpreter services (e.g., LanguageLine) in order to effectively communicate with non-English speakers. Remote interpreter services maintain their own code of confidentiality, but in addition to this, all interpreters will sign confidentiality agreements specific to RAPIDD.

Due to the variability inherent in disaster responses, the coordinating center, Social & Scientific Systems, Inc. (SSS), will determine and implement the most appropriate recruitment strategy based on the context of the situation. Only recruitment materials that have first received IRB approval will be used in the field.

4.1.2 Registry Visit

The registry visit may be scheduled, or the visit may occur unscheduled (e.g., during just-in-time training at the staging area) prior to deployment to the disaster area. The visit will consist of an explanation of the study and its expectations by a study staff member who is qualified and approved to obtain informed consent. The candidate will be allowed to ask questions and the study staff will allow ample time for the candidate to make an informed decision. Individuals who are eligible to participate and provide written consent will be enrolled, assigned a unique study ID number, and will undergo study procedures to collect baseline biological specimens, health information, or questionnaire responses according to **Table 1** in Section 6. Any additional study procedures will be described in Appendix B: Protocol Amendment Checklist during a protocol amendment process.

4.1.3 Visit Reminder Contacts

Most registry visits will occur immediately. In rare cases where a future visit has been scheduled with a participant, the study staff may use phone calls, email, or text reminders to inform a participant of the date and time of his/her upcoming visit at the work site or to confirm he/she will be able to attend.

4.1.4 Reports to Participants and Referrals

During each registry visit, study staff will collect measurements including: height and weight to calculate BMI, blood pressure, pulse oximetry and spirometry. The participant will receive handouts with the results of these tests/measurements, standardized clinical interpretations, and advice for seeking care (see Appendix E: Medical Referral Values and Recommended Actions). In addition to providing the participant with results, handouts and recommended actions, participants who do not have a primary care provider or who cannot afford to pay for care may be referred to a local clinic that provides care for services based on a sliding scale. The referral handout consists of a list of health resources and mental health resources including the DHHS Health Resources and Services Administration (HRSA) “Find a Health Center” search page and the Substance Abuse and Mental Health Services Administration (SAMHSA) treatment facility locator search page.

In the rare event where the clinical exam visit yields immediately actionable medical data (e.g., dangerously low/high blood pressure or O_2 saturation), trained study staff will immediately inform the coordinating center site manager and facilitate, if necessary, the administration of emergency care. The study staff will be responsible for ensuring appropriate follow-up care until the event resolves or stabilizes and the participant is under the care of a licensed medical provider.

It may be many years before participant samples are tested. Participants will not receive individual results from the future analysis of samples unless the analysis yields an abnormal value.

4.1.5 Registry Duration and Contact Updates

Once this cohort is registered, it is possible that the scientific community will be interested in conducting follow-up with this cohort for 10 years or longer depending on its size, what is learned from future analyses and scientific and/or public health need. Throughout the duration of the registry, we may occasionally email or send a letter to participants asking them to complete and return a form updating or confirming their contact information. Any mailings that are “returned to sender” will undergo tracing efforts to identify updated contact information. The participant will be informed when enrolling in this study that participation in future studies is voluntary.

4.2 Study Endpoints

A goal of the RAPIDD Study is to establish a well-characterized disaster response worker cohort that will allow for future analyses of associations between disaster exposures and health outcomes. While certain health outcomes in the disaster response worker cohort may be anticipated based on past disaster experience, the study is designed to allow for the investigation of a wide range of outcomes of interest for a given disaster scenario. These health outcomes may include, but are not limited to, the following areas: respiratory, cardiovascular, hematologic, dermatologic, neurologic, mental health, oncologic, reproductive, immunologic, hepatic and renal impacts.

5 Study Population

The population to be studied are disaster responders deployed to a disaster area to conduct emergency response activities. Disaster responders may include traditional first responders such as police, fire, and emergency medical personnel, as well as non-traditional responder groups such as public health personnel and workers involved in environmental remediation and restoration activities.

The following inclusion and exclusion criteria will be used to establish eligibility, and will be reviewed with participants prior to enrollment to verify eligibility. There are no enrollment restrictions with regard to gender, race, or ethnic background.

5.1 Participant Inclusion Criteria

At the time of screening, study candidates must meet **all** of the following inclusion criteria to be enrolled:

INCL 1. At least 21 years of age

INCL 2. Is part of an eligible disaster responder cohort as defined in Section 5 that has received IRB approval for inclusion

5.2 Participant Exclusion Criteria

Study candidates who meet the following exclusion criterion cannot be enrolled:

EXCL 1. Any conditions that, in the opinion of the Investigator, would pose an unacceptable risk to the participant or to the validity of the study results

6 Study Procedures

Table 1 List of Study Procedures

Procedure	Estimated Time (min)			Protocol Section
	Enhanced Set	Basic Set	Core Set	
Informed Consent	10	10	10	9.3
Vital Signs	2	2	N/A	6.1
Pulse Oximetry	2	2	N/A	6.2
Anthropometry	2	2	N/A	6.3
Spirometry*	15	N/A	N/A	6.4
Biospecimen Collection	30	15	5	6.5
Questionnaire Administration	20	10	5	6.11
Total Estimated Time	**81**	**41**	**20**	

*Only performed for participants who are eligible per the study inclusion/exclusion criteria (see Sections 5.1 and 5.2) after informed consent has been obtained (see Section 9.3).

All study procedures that may be included in the execution of this protocol during a specific disaster research response are outlined in **Table 1** and further described in Sections 6.1 – 6.11. In order to optimize flexibility, this protocol is scalable to a range of disaster situations. Three proposed sets of procedures (**enhanced, basic and core**), which vary by participant time burden, technical requirements, and available infrastructure, are described in the sub-sections below. In the early phases of disaster response when responder groups may have significant limitations in their available time for study, the core set of procedures option may be implemented which includes the self-collected biospecimen collection option (see Section 6.5.3) and the administration of a brief core registry questionnaire. We estimate that the core option would require 20 minutes of participant time. Conversely, the enhanced set of procedures option may be implemented in situations when responder groups have sufficient time available to allow a more comprehensive collection of health data and biospecimens (see Section 6.5.1). We estimate that the enhanced option would require approximately 80 minutes of participant time if consent for all study procedures are received and completed.

It is important to note that the composition of these procedure sets are only recommendations and may be revised at the time of the disaster to assure that the most appropriate set of study procedures for the situation are conducted. Our rationale for this standardized approach to procedural composition is that it allows us to develop in advance comprehensive specimen collection and processing documents, training manuals, along with materiel and equipment load lists so that these are readily available for the immediate research response to an evolving disaster. The specific set of procedures completed during a given disaster scenario may be a subset of these planned procedures. For example, workers may be without electrical power in the field, removing the option to collect samples that must be refrigerated or processed (e.g., centrifuged) on site. Study staff will refer to the Field Operations Guide (FOG) developed for each disaster for a description of the procedures from this protocol to be completed (and the order in which they will be completed) in the field.

While the planned procedures listed in **Table 1** represent a spectrum of data and specimens that would provide broad utility to future studies, it may be that novel procedures (e.g., dermal scrapings, neurobehavioral testing) are requested to investigate the unique circumstances of an individual disaster. In these situations, the RAPIDD study team will recommend an appropriate set of procedures and modify the RAPIDD protocol via the IRB amendment process. Study staff who administer the study procedures will have the necessary education, qualifications, and experience to conduct these activities. Study-specific training will be provided by the coordinating center (SSS) and research staff will be certified in each procedure administered in the protocol.

No specific diagnoses or pathology investigations are planned for the biological specimens or health information collected under this protocol. However, future research conducted under other research protocols may include such investigations.

All samples and data will be labeled and tracked using the participant's study ID. All participants will be asked to provide their contact information, age, gender, race, and ethnicity. The demographic questions are included in the core registry, basic health registry and enhanced health registry questionnaires (see Section 6.11). Age is the only demographic variable that determines eligibility. Data on gender, race, and ethnicity [required for National Institutes of Health (NIH) human participants reporting] are only used to characterize the study population.

No findings will be reported to the participant's employer (in fact, registry forms do not collect employer data) and it will be made clear to all participants, through the consent, that the RAPIDD Study does not supersede any occupational examination to determine fitness for deployment (i.e., participants cannot be included/excluded from deployment to a disaster response based on individual RAPIDD results) and that no testing for illegal drugs will be performed on participant samples.

6.1 Vital Signs

Vital signs recorded will include resting heart rate and blood pressure, which will be measured using standard clinical oscillometric equipment. In the core set of procedures option in **Table 1**, vital signs may be skipped to save participant time.

6.2 Pulse Oximetry

Oxygenation of the participant's hemoglobin will be measured using a pulse oximeter, with the sensor placed on a thin part of the body, such as a fingertip or earlobe. In the core set of procedures option, pulse oximetry may be eliminated to reduce participant time burden.

6.3 Anthropometry

Study staff will record measurements of weight (kg), height (cm), and hip and waist circumference (cm). Height will be measured with a portable stadiometer

or self-reported. Weight will be measured with a digital scale or self-reported. Hip and waist circumference will be measured with a reusable vinyl (or equivalent flexible) measuring tape.

6.3.1 Body Mass Index

Height and weight will be used to determine body mass index (BMI), which will be calculated according to one of the following equations:

$$\text{BMI} = \frac{\text{weight in kilograms}}{(\text{height in meters})^2} \quad \text{OR} \quad \frac{[\text{weight in pounds}] \times 703}{[(\text{height in inches})^2]}$$

6.4 Spirometry

Spirometry will be conducted according to American Thoracic Society (ATS) guidelines (6, 7).

Spirometry will be performed using a portable, transit time-based spirometer (e.g., EasyOne, ndd Medical Technologies, Inc., Andover, MA, USA, or a comparable model). All spirometers will undergo standard quality control checks each day they are used. A full Forced Vital Capacity (FVC) maneuver will be conducted to obtain three ATS-acceptable forced expiratory maneuvers, with a maximum of eight attempts allowed.

Spirometry will be conducted with the participant seated and wearing a disposable nose clip. New, individually-packaged, disposable mouthpieces and new spacers will be used for each participant.

To the extent possible, participants will be asked to not use their asthma inhalers on the day of the examination, and the timing and dosage of all asthma medications taken over the preceding seven days will be recorded.

Study staff conducting spirometry will be trained by coordinating center research staff familiar with collecting spirometric data in the field. Following training, staff will be required to submit 5 practice tests that are judged as acceptable by the pulmonary function testing software and will receive certification from coordinating center research staff. If computer-generated quality scores are lower than expected, coordinating center research staff will provide feedback along with suggested corrective actions to the study staff performing spirometry.

Exclusion from Undergoing Spirometry

Participants with a blood pressure >180 mmHg systolic or >110 mmHg diastolic, or with a heart rate >100 or <40 beats per minute will not undergo spirometry during the visit. Additionally, participants who answer yes to any of the following questions will also not be tested:

- In the past three months, have you had any surgery to your chest or abdomen?
- In the past three months, have you had a heart attack or stroke?

- In the past three months, have you had a detached retina or have you had eye surgery?
- In the past three months, have you been hospitalized for any other heart problem?
- Are you currently taking medication for tuberculosis?

These exclusion questions include those used in BOLD (8) and PLATINO (9), two multi-national studies that enrolled over 14,000 adults >40 years old for pre- and post-bronchodilator spirometry, administered by trained technicians. No adverse events occurred in either the BOLD or PLATINO studies. These exclusions are considered very conservative and these questions are not generally asked prior to spirometry maneuvers.

It is estimated that spirometric testing will require 15 minutes to conduct. In situations when available participant time is limited (basic and core sets), it may be skipped.

6.5 Biospecimen Collection

Table 2 Proposed Biospecimen Collection

Specimen Type	Collection Container	Enhanced Biospecimen Set	Basic Biospecimen Set	Core/Self-Collected Biospecimen Set	Protocol Section
Venous Blood	Red top tube, 10 mL	2			6.6
	Lavender top tube, 10 mL	2	1		
	Yellow top, 6 mL	1	1		
	Royal Blue top, 8 mL	1	1		
	PAXgene DNA (8.5 mL) OR PAXgene RNA (2.5mL)	1	1		
Urine	Cup, 100 mL	1	1	1	6.7
Hair	Foil Packet	1			6.8
Finger and/or Toenails	Envelope with dessicant	1			6.9
Oral Specimens	Salimetrics Oral Swab (saliva)	1			6.10
	Oragene: DNA or RNA, 2 mL (cells in saliva) OR Buccal Swabs			1	

As discussed in Section 6 above, we envision the selection of an appropriate mix of specimens for collection from a menu of three modular specimen sets (enhanced, basic and core). The decision of the most appropriate specimen set will be determined at the time of the event and will likely depend on the time available for collection as well as the availability of resources and infrastructure at the disaster site. As the event unfolds, if there are unique characteristics of the event or obvious adjustments in the mix of specimens that we are collecting,

it is very likely these can be made immediately, as long as new specimen types are not added to the mix (e.g., stool samples, dermatological scrapings, etc.) that would require procurement of different supplies and development of new collection or processing protocols.

Our proposed biospecimen collection schema is illustrated in **Table 2** which shows the appropriate collection container for each specimen type and the proposed number of containers to be collected for each biospecimen set. The specimen types and the rationale for their collection is discussed in more detail below.

6.5.1 Enhanced Set of Biospecimens

We propose to collect a full complement of biospecimens shown in **Table 2** in circumstances where study personnel will have easy and full access to potential study candidates with little or no time or resource constraints.

We believe that this approach will yield the broadest assortment of biological specimen types to provide researchers with optimal flexibility in the types of future analyses that they can perform. In this scenario, we would be collecting approximately 62 mL of blood of varying types and quantities as well as other biological samples designed to provide maximal testing flexibility.

There are two options available for collecting specimens for nucleic acid extraction. PreAnalytix (a Quiagen/Becton Dickinson company) makes two different PAXgene products for the immediate stabilization of DNA or RNA. Both of these tubes contain different quantities and types of proprietary diluents. The PAXgene DNA tube is designed to collect 8.5 mL of blood while the RNA tube (which contains more of the diluent) only collects 2.5 mL of blood. We suggest that DNA is more likely to be the desired nucleic acid component for extraction, but either tube, or both, can be provided in the collection set.

For this full complement of specimens, we assume that we would have a team of experienced and trained research assistants/phlebotomists who can collect *and process* these specimens under relatively controlled conditions. That is, there would need to be a sheltered space where data and specimen collection can occur (such as a tent, van/vehicle trailer, or building), and that electricity is available (access to commercial power or generator) so that blood specimens can be centrifuged and separated/aliquoted during processing. Also, this scenario requires the availability of some form of refrigeration, or access to (wet) ice, frozen ice packs, or possibly even dry ice (although dry ice is not an absolute requirement) for preservation of specimens during transport.

When collecting this full complement of biospecimens, we also assume that easy egress from the disaster area will be possible so that we can transport collected specimens to SSS' Central Processing Laboratory (CPL) in Durham or to other laboratories for analyses. Transport will be by commercial carriers (e.g., FedEx or UPS) if available, or by study personnel, or through other travel arrangements such as with local couriers. These research specimens will be properly packaged

for transport as *Exempt Human Specimens* according to DOT and IATA regulations.

We estimate that the approximate time required to collect the 10 biospecimens shown in **Table 2** will be 30 minutes (10 min for blood collection; 5 min each for urine, toenails, hair, and saliva). Processing, aliquoting and preparation of collected specimens for transport will also require time to complete, but this will not be at a burden to study participants.

6.5.2 Basic Set of Biospecimens

In circumstances where the time available to collect biospecimens is limited, or when there are resource (e.g., loss of power) or accessibility constraints, we propose to collect a reduced number of specimens as shown in **Table 2**. The most obvious differences in this assortment of biospecimens is that we would not collect red top tubes, and we would collect one fewer lavender top tube. This is because in order to be able to harvest serum from these tubes, they must be centrifuged, which requires electrical power. The remaining tube types (lavender, yellow, royal blue, and PAXgene tubes) do not require centrifugation and separation to yield usable specimens, and can be stored under ambient condition for several days (lavender and yellow top tubes) or for many months (remaining tubes) before additional processing or analyses is necessary.

For this option we would still need to provide experienced and trained phlebotomists to do the blood collections, but little or no specimen processing will be required. Biospecimens will just need to be properly packaged for immediate or delayed shipment to our CPL for further processing and long-term storage.

Collection of three fewer tubes of blood also shortens the total blood collection time by approximately 2-3 minutes. To further shorten the time that a participant needs to spend having biospecimens collected, we suggest that hair and nail collections can be eliminated, as these slow-growing biospecimens could be collected later and still provide valuable baseline information.

Regarding the oral specimens, we also suggest eliminating collection of the SOS swab that was included under the full complement (enhanced) biospecimen set. The SOS device is designed to provide saliva for either endocrine or metabolic studies, but *not* for collection of cells for DNA isolation. If we are able to get any blood specimens at all, we will have more than sufficient DNA available for extraction from these blood specimens if needed. Elimination of the need for collection a saliva sample for metabolic studies further reduces the time needed for biospecimen collection to approximately 15 minutes overall.

6.5.3 Core Set of Biospecimens (Self-Collected)

In those rapidly evolving situations where very little time is available for workers to participate in research activities. We suggest that participants may be able to self-collect a few “core” biospecimens that may be of some research value. Our research staff will provide sterile urine collection cups and one of two different

types of oral specimen collection devices. These oral specimen collection devices are discussed in more detail below. Since blood is not being collected under this scenario, these oral samples provide a means of obtaining a limited quantity of cells for eventual DNA or RNA extraction. Collection of these two specimens would require less than 10 minutes and would not require the presence of experienced, trained collectors. We have developed very simple participant instructions for collection of these specimens in our Field Operations Guide to be distributed to participants that have agreed to submit self-collected biospecimens. Participants will be asked to return these biospecimens immediately after self-collection to coordinating center staff at the research site.

6.6 Venipuncture

We will collect peripheral blood by venipuncture using standard phlebotomy techniques and blood collection supplies by appropriately trained and experienced staff. The amount of blood collected will not exceed 65 mL for any participant.

The type of tubes into which the blood is collected is provided in **Table 2** and are described in more detail below:

- Up to two 10 mL red-top tubes, with no additives and no separator gel, may be collected depending on the scenarios described above. After clotting, and with the availability of power, research personnel will separate the serum and clots by centrifugation. These specimens will be packaged for cold shipment to the CPL, or they can be frozen if dry ice or freezers are available locally for short term storage.
- Up to two 10-mL lavender-top tubes containing K_2EDTA to prevent clotting may be collected. With the availability of power for centrifugation our research personnel will separate the plasma from the packed cells and package them for immediate shipment to the CPL. If the specimens cannot be centrifuged, they can either be shipped unspun to the CPL, or they can be held locally at ambient temperature for short periods, or they can be cryopreserved and frozen if resources are available.
- One 6 mL yellow-top tube containing Acid/Citrate/Dextrose Solution B may be collected for preservation of white blood cells. Leukocyte viability is maintained at ambient temperature for up to 2 or 3 days, but for optimum recovery and DNA extraction, these specimens should be processed as soon as possible. Hence, they are very dependent on the availability of overnight specimen transport capability so that they can be processed as soon as practical in the CPL. With the availability of freezers or dry ice, research personnel in the field may be able to cryopreserve the whole blood specimen to preserve leukocytes for future DNA/RNA extraction.
- One 6-mL Royal Blue tube preserved with K_2EDTA tube may be collected for trace metal analyses. These tubes are certified by the manufacturer to contain less than the quantities (micrograms/L) of the following trace

metals:

- Arsenic 0.2
- Cadmium 0.1
- Calcium 150.0
- Chromium 0.5
- Copper 5.0
- Iron 25.0
- Lead 0.3
- Magnesium 40.0
- Manganese 1.5
- Mercury 3.0
- Selenium 0.6
- Zinc 40.0

These specimens can be held at ambient temperature for several days if necessary. Our research personnel will package them for transport to our CPL or temporarily store them locally. If freezers are available, the tubes will be carefully frozen in the original unopened collection tube (to protect trace metal integrity) at -20°C for future transport or measurement of metals. Either PAXgene DNA or RNA tubes can be collected, or both. Since the diluent in these tubes immediately stabilizes the nucleotides, they can be held at ambient temperature for prolonged intervals (years) before they have to be extracted and analyzed. We will ship these blood specimens to the CPL for processing and long-term storage as transport is available.

In the event that a participant has poor venous access, study staff will attempt blood draw up to two times per arm if the participant agrees. If only a partial blood tube is collected due to a temporary interruption in the collection procedure, the partially filled tube will be retained. If we are unable to collect blood, we may ask the participant to obtain an Oragene saliva cell sample or buccal swab as discussed in Section 6.10 below.

6.7 Urine Collection

Participants may be asked to provide a (“spot”) urine sample in a sterile container using the mid-stream catch technique. Since urine collection cups do not always transport well, research personnel will aliquot the specimen into sturdier 50 mL screw-cap transport tubes, and may opt to preserve a portion of the specimen in urine preservative tubes (e.g., BD 364943). These urine preservative tubes contain stabilizing agents such as sodium propionate, ethyl paraben, and chlorhexidine to prevent bacterial overgrowth or bacterial metabolism of possible urine analytes of interest.

6.8 Hair Collection

If the study participant has nape hair that is at least 1 cm long, research personnel may collect a small hair sample as close to the participant’s scalp as possible. Research personnel will clip and mark hair samples to indicate which end of the clipped hair sample was closest to the scalp. We will temporarily store these hair samples at ambient temperature prior to shipping. For long-term storage of samples, our CPL will store these hair clippings at -20°C for future analyses.

6.9 Nail Clipping Collection

Fingernail or toenail clippings may be collected for future analysis. Toenails are preferred over fingernails as these grow slower. Nail polish on the nails should be removed prior to clipping. The nail clippings will temporarily be stored at ambient temperature with a desiccant prior to shipping samples for long-term storage and future analysis. For the long term storage of samples, nail clippings will be stored, with desiccant, at -20°C. As noted above, we may provide participants with self-collection kits, simple instructions, and mailers so that nail clippings can be collected at the participant's convenience at some future time.

6.10 Oral Specimens

Both saliva and oral epithelial cells can be self-collected by study participants. Whereas DNA can be collected from the buccal epithelial cells, saliva can be used for both endocrine and metabolic studies. There are a variety of collection devices that are designed for easy, non-invasive specimen collection that can be used by the participant with minimal instruction.

6.10.1 Salimetrics' SalivaBio Oral Swab (SOS) for Saliva Collection

Salimetrics' SalivaBio Oral Swab (SOS) kits are designed for collection of approximately 2 mL of saliva for endocrine or metabolic testing. These devices are not designed for collection of oral cells for genetic or molecular studies. We have proposed that research personnel have study participants collect a saliva sample as a component of the Enhanced Biospecimen set, as this provides another sample matrix that may be useful for future research. Collection of a saliva specimen as part of the enhanced biospecimen set can serve a two-fold purpose. Not only does this provide a basefline saliva specimen but it also trains the participant on the proper way to collect this specimen under the observation of our trained research personnel. Thus, if we desire to collect a series of timed saliva specimens from the participant at some point in the future, the participants will recall how to properly collect the specimen and we will have a point of comparison. SSS has prepared easy-to-use, color-coded, timed specimen collection instructions, a saliva specimen holder, a simple specimen collection diary/questionnaire, and a prepaid shipper that has successfully been used for collection of hundreds of timed specimens from participants in other NIEHS studies.

6.10.2 Oragene DNA or RNA Collection Devices

These devices provide a simple all-in-one system for the collection and transportation of saliva ladened with buccal cells and leukocytes which can be used for future DNA or RNA extraction. The quantity of DNA obtained through these devices is less than what can be obtained from blood specimens, but can provide sufficient material for some genetic or molecular analyses. The Oragene

device contains a proprietary diluent that stabilizes nucleic acids in the specimen for up to a year or more at ambient temperature.

Prior to collecting a saliva specimen participants should not eat, smoke, or chew gum for at least 30 minutes prior to collection. Participants are instructed to expel saliva into an Oragene OGR500 collection device until the sample amount reaches a marked 2 mL fill line on the container. After sample collection, a member of the research staff or participant will close the container, screw the cap on tightly (which releases a proprietary preservative that is stored in the lid), and gently shake the sample kit gently for 10 seconds. While in the field or during transport, these specimens will be stored at ambient conditions. Once the Oragene devices are returned to the central processing laboratory, for conservation of space and greater stability for longer-term storage, we recommend that unpurified Oragene/saliva samples be heat inactivated at 50°C for 60 minutes and then aliquoted into 1 mL cryovials for long-term storage of these saliva aliquots at -80°C or in liquid nitrogen vapor for future use.

6.10.3 Buccal Cell Collection

As an alternative to the Oragene, study staff may use an Isohelix DNA Buccal Swab SK-1 to scrape/rub the inside of the participant's mouth (cheek) with firm pressure 10 times in succession or for at least 30-60 seconds. The swab/brush head will be placed into a tube along with either an Isohelix Dri-Capsule or with added DSK Stabilising and Lysis Kit reagent to stabilize the harvested cells. Specimens will be stored at 4°C. DNA may be purified immediately or samples may be stored on the collection swab for up to three to five years at room temperature (15–25°C). Although the Isohelix swab collects more oral cells (primarily epithelial cells with some leukocytes) then the Oragene kit, variation can result from the force applied to the brush during collection which can affect the number of cells collected. Buccal swabs tend to have a higher level of contamination with bacterial DNA. Preservation of buccal cells requires the addition of the stabilizing agents to the storage tube after collection.

6.11 Questionnaire Administration

Study staff will administer questionnaires aimed at collecting contact information, demographic variables, information about general/overall health (including mental health), environmental exposures, lifestyle, or sociological parameters.

The set of instruments that may be used is described in Appendix C: Questionnaires Available for RAPIDD. Included are three questionnaires (a brief core registry questionnaire to obtain contact information when time and/or availability is severely limited, a basic health registry form when there is more time available for interview and an enhanced health registry form when there is even greater flexibility in time and/or availability or additional data points are desired), which may be used to collect general health registry/contact information.

A disaster situation may occur that results in a need to modify or add one or more questionnaires to the appendix. In such situations, the study team will convene the necessary experts who are able to help modify the questionnaires or recommend alternate options for collecting information. For example, collection of exposure information may be critical during the cleanup of a chemical spill; in that case, experts with knowledge of the particular chemical involved, expected risks from exposure to it, and what health effects to monitor would be consulted to ensure the study team collects the type of information that would be most pertinent to future researchers who want to use this information.

The study team will ensure IRB approval is in place prior to the use of any modified or new questionnaire materials.

6.12 Additional Procedures

Additional specimens or data may be requested from participants to supplement the proposed procedures described above. All additional procedures will be described in Appendix B: Protocol Amendment Checklist along with any known risks. IRB review and approval is required before any such additional procedures may be performed.

7 Collection and Storage of Human Specimens or Data

7.1 Handling of Samples During Initial Collection and Processing

Because transmission of HIV and other blood-borne pathogens can occur through contact with contaminated needles, blood, blood products, and body secretions, appropriate protective precautions will be employed by all personnel in the collection of biological specimens and shipping and handling of all specimens for this study, as currently recommended by the CDC and the NIH.

All specimens will be transported using packaging mandated in the Code of Federal Regulations (CFR), 42 CFR Part 72, and according to individual carrier guidelines, as applicable.

In rare instances that freezer facilities are available at the collection site, samples being stored on-site at -80°C will be shipped on dry ice if at all possible, while samples being stored on-site at -20°C will be shipped in a container maintaining a temperature of approximately -20°C through the use of frozen refrigerant packs (such as foam phase change materials). Refrigerated and/or ambient temperature samples may be shipped on wet ice or with refrigerant packs. Specimens stored at ambient temperature can also be shipped at ambient temperature.

Prior to the transfer of the specimens to a long-term storage facility or biorepository, the biological samples may initially transferred from the study site to a central processing laboratory (CPL) that has adequate processing and short-term storage capabilities, such as the laboratory that is a component of the coordinating center for this protocol (SSS).

Once the specimens have arrived at the CPL, they will undergo any additional processing and will be prepared for long-term storage. Aliquots will be divided and stored using liquid nitrogen and -20°C/-80°C mechanical freezers as appropriate for each sample to ensure the integrity of the samples. The CPL will prepare the accumulated samples for bulk transport to the NIEHS biorepository (or appropriate NIEHS-contracted facility) for long-term storage, with transfer of the samples to the repository targeted to occur within one week of receipt at the CPL.

The NIEHS repository is located in Keystone Park, in the Research Triangle Park, North Carolina, near the NIEHS campus and within 2 miles of SSS CPL. The NIEHS Biorepository provides qualified personnel, materials, equipment and facilities for the receipt and long-term, secure storage of research specimens at temperatures ranging from humidity controlled ambient temperature all the way down to liquid nitrogen temperatures (-193°C).

7.2 Intended Use of Stored Specimens/Data

During this study, biological specimens (e.g., blood, urine, nail clippings, saliva, buccal cells, hair) or participant data (e.g., spirometry test results, questionnaire responses) will be collected and stored for future health-related scientific investigations into disaster responses, which may be conducted by investigators within or outside the NIH. All requests for samples and data will be reviewed according to current NIEHS policies and will be evaluated by the appropriate review committee(s) as required (see Section 11.6). Requests for specimens/data must include a detailed proposal and proof of appropriate IRB approvals.

Fully-executed Material Transfer Agreements and/or Data Use/Transfer Agreements will be required before specimens or data are released. Once appropriate approvals and agreements are in place, the NIEHS study team may send the requested materials along with a coded label that can be traced to the participant only by the study team.

There is no intent to place the results of any investigational analyses into the participants' medical records.

7.3 Methods of Storing Specimens/Data

Collected specimens and data will initially be coded, using codes assigned by the investigator, and stored at a secure site (i.e., any short-term or long-term storage facilities must be secured).

Specimens will be stored in a restricted-access freezer. Electronic data will be kept in password-protected computers; paper data sources will be stored in a locked file cabinet. Only designated study staff and approved collaborators will have access to the samples and data.

7.4 Long-Term Handling of Samples/Data

All samples and data will be retained indefinitely to be available for further study by approved researchers. Samples or data will only be destroyed at the written request of study participants (see Section 7.5).

7.5 Loss or Destruction of Samples/Data

Participants may decide at any point not to have their specimens or data stored. In this case, the samples or data will be destroyed after the participant has provided a written request to do so, which includes a description of which samples or data should be destroyed. Once the written request is received, the PI will have the applicable samples/data destroyed and report what was done to both the participant and to the IRB. This decision will not affect the individual's participation in this protocol or any other protocols at NIH.

Any loss or unanticipated destruction of samples or data that meets the NIH Intramural Protocol Deviation definition, or results in a deviation that compromises the scientific integrity of the data collected for the study will be reported to the NIEHS IRB.

8 Statistical Considerations

8.1 Data Analysis

Descriptive statistics will be used to characterize the sociodemographic, health, and lifestyle information of enrolled participants. Standard deviations, means, medians, and interquartile ranges will be used to summarize continuous variables. Rates and proportions will be estimated for discrete variables and bivariate relationships will be explored using cross tabulations. 95% confidence intervals (CIs) will be estimated where appropriate. Propensity score weighting or matching can be used in subsequent health effects analyses if the descriptive data indicate that the enrolled population is not representative of the target population.

Relationships between exposures or disaster-related activities and health outcomes can be investigated by fitting regression models. Logistic regression models can be used for dichotomous outcomes to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for each exposure. Least squares regression can be used for continuous outcomes to estimate effect parameters and standard errors (SEs) for each exposure. Outcomes may include a range of doctor-diagnosed general and physical health outcomes, clinical measurements of health status (e.g. pulmonary or neurobehavioral function), and self-reported health status and disease-related symptoms. Relevant demographic variables (e.g., gender, age, race, socioeconomic status indicators) and other exposures will be included in the regression models as covariates and effect modifiers. Various refinements to these basic methods, as well as additional analytical approaches, will also be pursued as appropriate. Stratified analyses will be used when there is evidence of effect modification (interaction), i.e., when

the exposure-health outcome associations differ across levels of a covariate (e.g., SES, age, etc.)

8.2 Sample Size

This study is designed not around a few narrow *a priori* hypotheses, but rather to allow the investigation of a wide range of potential adverse exposure scenarios and related health effects. Thus, a wide range of exposure scenarios and possible health effects is considered in the power analysis. We anticipate enrolling disaster response workers deployed to a federally declared disaster area to conduct emergency response activities where a portion of the workers will experience a given exposure. The study size and the number of individuals who are exposed – and the statistical power – will largely be determined by the number of individuals impacted by the disaster. For dichotomous health outcomes, **Table 3** presents minimum detectable odds ratios across a range of proportions of workers with "high" exposure and a range of proportions of workers with "low" exposure (the referent group). Given that all participants will be workers and the types and levels of exposure will vary by the type of disaster and type of job, "high" exposure and "low" exposure (referent group) will be determined in the context of the individual studies. This may be based on established cut points or, in the absence of established scientific or clinical guidelines, on quartiles (e.g. highest vs. lowest quartile). The power analysis in **Table 3** is based on an α of 0.05, power of 80%, and a two-sided Pearson chi-square test for two proportions, which is likely to be more conservative than a logistic regression analysis including covariates.

Table 3 Minimum detectable odds ratio for dichotomous health outcomes for a range of proportions of participants with "high" exposure in the disaster and a range of proportions of health outcomes among participants in the referent group. N is the total number of participants.

		Minimum Detectable Odds Ratio (OR)					
Proportion in Referent Group with Health Outcome	**Proportion of Sample with "High" Exposure**	**N =250**	**N =500**	**N = 1,000**	**N = 2,000**	**N = 5,000**	**N = 10,000**
3%	**5%**	10.65	6.56	4.44	3.21	2.27	1.86
	10%	7.14	4.71	3.34	2.52	1.89	1.61
	25%	4.99	3.43	2.55	2.02	1.60	1.41
	50%	4.58	3.17	2.37	1.89	1.53	1.36
	75%	5.78	3.81	2.73	2.10	1.63	1.43
	90%	10.08	6.06	3.96	2.81	2.00	1.66
5%	**5%**	8.19	5.15	3.59	2.67	1.97	1.66
	10%	5.51	3.76	2.76	2.16	1.68	1.47
	25%	3.90	2.80	2.17	1.77	1.46	1.32
	50%	3.55	2.58	2.02	1.68	1.40	1.28
	75%	4.33	3.01	2.26	1.82	1.48	1.33
	90%	7.16	4.52	3.11	2.32	1.74	1.50
10%	**5%**	6.13	3.94	2.83	2.19	1.70	1.47
	10%	4.14	2.93	2.24	1.82	1.49	1.34
	25%	2.97	2.25	1.82	1.55	1.33	1.23
	50%	2.71	2.08	1.71	1.47	1.29	1.20
	75%	3.16	2.34	1.86	1.57	1.34	1.23
	90%	4.86	3.27	2.40	1.89	1.52	1.35
30%	**5%**	5.09	3.12	2.26	1.80	1.46	1.31
	10%	3.24	2.32	1.83	1.54	1.32	1.22
	25%	2.31	1.82	1.53	1.36	1.22	1.15
	50%	2.08	1.69	1.45	1.31	1.19	1.13
	75%	2.33	1.83	1.54	1.36	1.22	1.15
	90%	3.32	2.37	1.86	1.56	1.33	1.22

When the sample size is relatively large (≥ 2000), odds ratios of less than 2.00 can be detected, except when the health outcomes are rare and the proportion of participants in the "high" exposure group is very small or very large. In general, larger sample sizes are required for health outcomes that are rare, while smaller sample sizes are adequate for health outcomes with a higher prevalence, especially when the sample sizes are balanced between the exposed and referent groups.

For continuous health outcomes, **Table 4** presents minimum detectable mean differences, in standard deviations, across a range of proportions of exposure among enrolled participants. The power analysis in **Table 4** is based on an α of 0.05, power of 80%, and a two-sided t-test, which is likely to be more conservative than a multivariate regression analysis including covariates.

Table 4. Minimum detectable mean differences, in standard deviations, for continuous health outcomes for a range of proportions of participants exposed in the disaster. N is the total number of participants.

Proportion of Total Sample with "High" Exposure	Minimum Detectable Mean Difference					
	N = 250	N = 500	N = 1,000	N = 2,000	N = 5,000	N =10,000
5%	0.83	0.58	0.41	0.29	0.18	0.13
10%	0.59	0.42	0.30	0.21	0.13	0.09
25%	0.41	0.29	0.21	0.15	0.09	0.06
50%	0.36	0.25	0.18	0.13	0.08	0.06
75%	0.41	0.29	0.21	0.15	0.09	0.06
90%	0.59	0.42	0.30	0.29	0.13	0.09

When the sample size is relatively large (≥ 1000), then a study has power to detect mean differences of 0.5 standard deviations or smaller. The smallest minimum detectable mean differences occur when the sample sizes are balanced between the "high" exposure and the referent groups.

9 Protection of Human Subjects

9.1 Investigator Responsibilities

The Principal Investigator (PI) will:

- Submit the protocol, informed consent form, proposed recruitment materials, and any other materials for participants to the NIEHS IRB for review and approval, and ensure that participants are not enrolled until the submission has been approved in writing by the IRB
- Submit a written report to the IRB within 60 days of protocol implementation outlining response rates, evaluation of procedures, adverse events etc. (see Appendix F for full list of report elements)
- Obtain IRB approval of the annual Continuing Review for the duration of the study

- Obtain IRB approval for all amendments to the protocol, informed consent form, and other study documentation referenced above and ensure that amendments are not implemented without prior IRB approval
- Monitor and evaluate study progress, including periodic assessments of accrual, administration of informed consent, data quality, timeliness of data collection, participant risk versus benefit, performance of contractors, and other factors that can affect study outcomes (including external variables that may be related to the study, such as scientific findings that may have an impact on the safety of the participants or the ethics of the study)
- Track and appropriately report Unanticipated Problems (UPs), Protocol Deviations (PDs), Adverse Events (AEs), deaths, withdrawal of consent for sample storage, and early study termination, in accordance with NIEHS IRB policies and applicable NIH SOPs (e.g., NIH HRPP SOP 16 "Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations"); in particular, the PI will report all Serious UPs, Serious PDs, and Serious AEs to the NIEHS IRB and NIEHS Clinical Director as soon as possible, but not more than 7 days after the PI first learns of the event.

9.2 Coordinating Center Responsibilities

Social & Scientific Systems, Inc. (SSS), a company that provides professional research services, will serve as the coordinating center and will function in a supportive and collaborative role through an existing contract with the NIEHS.

The coordinating center will be responsible for creating required study documents, conducting training, developing and implementing operational plans and study procedures, data management, study monitoring, and the performance of subcontractors who support ancillary research activities. Activities of the coordinating center will be conducted in collaboration with the PI and any relevant expert consultants.

Research study staff from the coordinating center will have the necessary education, qualifications, and experience to conduct all research study activities. Study staff will be required to undergo pre-employment screening and produce credentials commensurate with the anticipated level of complexity. After hire, they will receive training in human subjects' protection, CPR, blood borne pathogens, data security, ethics, and study specific training modules including disaster specific health and safety training, informed consent administrations, procedural conduct, questionnaire administration, distressed participant training, and others. Training requirements and conduct are covered in the Field Operations Guide. Staff will be required to complete training programs specific to their roles in the project, pass proficiency testing, and receive certification prior to conducting study procedures. Our current intramural research team is led by personnel with previous disaster response experience including 9/11 in New York City, Hurricanes Katrina, Charlie and Wilma, pandemic influenza response,

HazMat response, and the GuLF STUDY. All study staff will be required to sign confidentiality agreements.

Data managers at the coordinating center will generate data Quality Control (QC) reports that will allow the study investigators and coordinating center staff to identify problems with missing, inconsistent, or otherwise implausible data so that any problems with data quality can be identified and corrected in a timely manner. In situations when completion of missing individual data is desired, the RAPIDD study team reserves the right to re-contact participants. All participants are informed of the possibility of follow-up during the consenting process.

Study managers at the coordinating center will monitor accrual and procedural completion data, review QC assessment forms quarterly, and coordinate site monitoring visits as part of the overall quality control process. Study managers will conduct periodic quality control assessments of staff performance using standardized quality control checklists and will provide feedback to staff. Corrective actions for unsatisfactory performance will include coaching, retraining, or termination. The PI will review unanticipated problems, adverse events, and protocol deviations as they occur, and they will also be reviewed in aggregate at least annually to identify any negative trends.

Study monitoring will occur in accordance with NIEHS requirements, and will be performed to ensure compliance with the protocol, NIEHS research policies, and federal regulations for the protection of human subjects (see Section 10.1).

9.3 Informed Consent Administration

The PI is responsible for ensuring informed consent is obtained from all participants and properly documented in compliance with 45 CFR 46.

A one-page consent form summary will be used to guide the informed consent process. To help potential participants make an informed decision about enrollment, the designated study staff, trained in informed consent administration, will discuss the study's purpose, duration of participation, procedures, risks, benefits, record confidentiality, how to contact study personnel, and the rights of participants. Potential participants will be given ample time to ask questions and obtain clarifications regarding the study prior to agreeing to enroll. Bilingual study staff will be available to work with non-English speaking participants for common foreign languages (e.g., Spanish) likely to be encountered. The study team may also use remote interpreter services in order to effectively communicate with non-English speakers so they can make an informed decision about participation.

After voluntarily agreeing to take part in the study, participants will be asked to sign and date a current IRB-approved informed consent form (ICF), and will be given a copy of the signed and dated document. The signed ICF will be obtained prior to the initiation of any study procedures. Participants will be informed that they may withdraw consent at any time throughout the study. Participants will also be informed that they may be contacted by future researchers for follow-up studies and that participation in follow-up studies is completely voluntary and will

not affect their participation in this protocol. The consent form will contain contact information for coordinating center staff and the NIEHS IRB in the event that questions or concerns emerge after the visit. The original version of the ICF will be retained in the study files. Random review of consent forms will be included in the study's clinical monitoring plan (Section 10.1).

Participants will be informed of any changes in the design or risks of the study that could impact the participant (e.g., a change in the risk for breach of confidentiality).

9.4 Evaluation of Risks/Discomforts and Benefits Ratio

9.4.1 Potential Benefits

Participation in this study is not anticipated to provide any direct benefit to a participant's overall health or any existing medical conditions.

Study participants may benefit from the positive feelings associated with participating in a study that explores the health effects of a disaster that may add value to their community. The knowledge gained from this study may have a significant impact on future public health responses to disasters. It is also possible that participants may benefit directly from public health responses that are based on early findings from research conducted using samples and data collected during this study. Additionally, participants may benefit from receiving the results from the registry exam which they can share with their physician or healthcare provider.

9.4.2 Potential Risks

The proposed study presents minimal risk to participants. Adverse events associated with study procedures are expected to be uncommon and limited to mild and transient discomforts. In order to minimize risks to participants, qualified, experienced, and well-trained research staff will conduct all study procedures. Possible known risks are described in the following sub-sections.

9.4.3 Risks Associated with Spirometry

Spirometry is a very low-risk procedure with few side effects. Participants may experience transient coughing, lightheadedness, dizziness, fainting (more commonly in older persons with impaired lung function), and chest tightness. These symptoms usually resolve after the test is complete.

To minimize risks associated with this procedure, very conservative exclusions for undergoing spirometry will be implemented, testing is done in a seated position, and study personnel will be trained to look for signs of dizziness or other problems and will stop the maneuver if necessary.

Any risk of transmitting infection from one participant to the next through the use of shared equipment is minimized by using disposable nose clips, spacers, and

mouthpieces (spirettes), which have the additional protection of a built-in bacterial filter.

9.4.4 Risks Associated with Venipuncture

Peripheral blood sampling entails a risk of mild discomfort, bleeding, bruising, with infrequent hematoma formation, vein irritation, or infection from the venipuncture, and a possibility of lightheadedness or fainting.

To minimize risks associated with this procedure, the amount of blood drawn will be limited to no more than 100 mL, study staff who are appropriately trained in phlebotomy will perform this procedure, and attempts to draw blood will be limited to up to three attempts if the participant agrees.

9.4.5 Risks Associated with Collection of Nail Clippings, Hair, Saliva, and Buccal Cells

Collection of nail clippings, hair, saliva, and buccal cells are all very low-risk procedures with few side effects. Participants may rarely experience mild local trauma or infection at the collection site.

Although no specific genetics research is planned under this protocol, if DNA is isolated from these samples by future researchers for genetic analyses, the risks associated with genetics research may apply. This includes breach of confidentiality of test results that could result in impacts on employability, insurability, discrimination, or psychosocial risks to the participant or participant's family.

9.4.6 Risks Associated with Questionnaire Administration

The questionnaires used for this study are based on instruments that are widely used in epidemiological studies and disaster research and have been evaluated for their reliability, validity, ease of use and overall low participant burden. All mental health questions included in the core questionnaires listed in Appendix C have been previously reviewed and approved by the NIEHS IRB for use in other studies.

The main risk in questionnaire administration involves discomfort around sensitive health topics or personal experiences that may be traumatic; in some cases such questions could trigger emotions, stress, or other reactions that are difficult or painful for the participant to experience (e.g., post-traumatic stress disorder). To help minimize this risk, participants will be told that they may skip any or all questions or end the interview at any time. Also, to the extent possible at the study site, a private setting for completing sensitive surveys or interviews will be provided. Further, field staff receive training in handing emotionally difficult situations and have a list of mental health referral sources available to participants in distress.

9.4.7 Other Risks, Loss of Privacy, and Breach of Confidentiality

No risks are anticipated for other study procedures, with the exception of the potential for loss of privacy or breach of confidentiality as a result of inadvertent disclosure of information collected for research purposes (e.g., de-identified data distributed through controlled-access procedures could be linked back to a participant in ways that cannot be foreseen at present). To help minimize the risk of forced disclosure of information that could identify a participant, the study team will obtain a Certificate of Confidentiality (see Section 9.5.1).

Participants will be informed about the possibility for loss of privacy or breach of confidentiality. We will not collect information about the participant's employer. Participants will be informed that since employer information will not be collected, the study team cannot share their personal study information with their employer., However, there may still be some risk of adverse outcomes should any results of tests or procedures that indicate physical or mental health problems be inadvertently acquired by a participant's employer.

Measures to protect privacy and confidentiality are further described in Section 9.5.

Participants will be informed of any health information learned in course of conducting study procedures indicative of an immediate risk to the health or safety of the participant (e.g., extremely high blood pressure or resting heart rate in a deployed worker engaged in strenuous physical activity).

Finally, if any procedures or evaluations are added to this protocol per Section 6, they will be listed and their risks described in Appendix B: Protocol Amendment Checklist.

9.5 Protection of Participants' Privacy and Confidentiality

The PI is responsible for ensuring that the participants' privacy and confidentiality is maintained. All records will be kept confidential to the extent provided by federal, state, and local law. Only study staff will have routine access to study records and data. In situations where data collection takes place in multiple sites, study staff will only have access to site-specific data (i.e., only central coordinating center staff will have full access to multi-site data). Research samples, electronic case report forms (eCRFs), and other research documents will be coded with a unique participant identification number and will not include personally identifiable information (PII) to the extent possible (e.g., some questionnaires may collect PII). The results of the study may be presented in reports, published in scientific journals, or presented at medical meetings. However, participants will not be identified in any study reports.

Study information will be kept secure and private in two locations as follows:

- Hard copies of the signed consent forms and any paper data collection tools will be kept in a locked study file cabinet

- Electronic records with personal identifying information, such as name, address and phone number and other data collected as part of the study procedures will be stored in a password-protected study management database

Clinical information will not be released without written permission of the participant, except as necessary for monitoring by the IRB, NIEHS, and Office of Human Research Protection (OHRP). The investigator will inform participants that study monitors and other representatives of the NIEHS may inspect research records. Participants will also be informed that study monitors and other NIEHS representatives are bound by agreement and the law to maintain participant privacy and confidentiality.

9.5.1 Certificate of Confidentiality

To help safeguard the privacy of human research participants enrolled in this study, the study team will obtain a Certificate of Confidentiality to protect against compulsory legal demands (e.g., a court subpoena, or any federal, state, or local civil, criminal, administrative, legislative, or other proceedings) for identifying information or identifying characteristics of any research participants.

9.6 Study Discontinuation

Participants may voluntarily withdraw from the study at any time. Participants will be informed that unless explicit written instructions are received, investigators will continue to use data and samples collected up to the point of withdrawal. Study staff will effectively destroy all known remaining samples by anonymizing the samples using a newly assigned ID number and report what was done to both the subject and to the IRB. This decision will not affect the subject's participation in this protocol or any other protocols at NIH. Anonymizing the samples will effectively terminate any association the samples have with the study participant, fulfilling their request, while simultaneously providing samples that can be used for laboratory QA/QC procedures. However, should the subject specifically request it in writing, we will physically destroy all remaining samples.

Study staff will seek feedback from the participant to determine reasons for discontinuation and to identify any barriers that can be addressed to keep the participant in the study. The reasons for all discontinuations will be recorded in the data collection system and routinely monitored by the investigator. Common barriers to ongoing participation may be addressed by changes in retention strategies or study design.

10 Data and Safety Monitoring Plan

The PI will be responsible for ensuring the safety of research subjects and the integrity of research data, consistent with regulatory and NIH requirements.

There is minimal risk associated with the study procedures and evaluations, and the main objective of this study is to create a repository of specimens and data.

Thus, the nature of this study does not warrant the use of a Data and Safety Monitoring Board (DSMB).

Prior to implementation of this study, the protocol, the proposed patient consent forms, and any other patient materials (additional materials are listed in Appendix A: List of Appendices) will be reviewed and approved by the NIEHS IRB, according to 45 CFR 46. After study implementation, the NIEHS IRB requires that the study team report back to the Board within 60 days of study initiation regarding any study activities that impact the safety of research subjects. A template for the Review of RAPIDD Protocol Implementation Report has been developed and is available in Appendix F. The NIEHS IRB must receive and approve this report in order for the RAPIDD study to continue enrolling new participants.

The NIEHS IRB will approve all amendments to the protocol or informed consent, and will conduct continuing annual reviews so long as the protocol is open to accrual or sample/data storage continues under this protocol.

10.1 Clinical Monitoring Plan

The coordinating center will designate an independent clinical monitor to carry out monitoring visits. The purpose of the visits is to ensure that the rights of human participants are protected, that the study is implemented in accordance with the protocol and NIEHS standards, and that the integrity of study samples and data are maintained. The monitor will review various aspects of the study including, but not limited to:

- Documentation of informed consent
- Compliance with the protocol
- Documentation and reporting of unanticipated problems, adverse events, and protocol deviations
- Handling and storage of biological specimens
- Completeness and accuracy of study data

The scheduling and frequency of monitoring visits will depend on the date the first participant is enrolled, the rate of enrollment, and the anticipated duration of operations at a given study site. The monitor, in conjunction with the coordinating center, will work with the site manager or investigator to schedule the visits at a time that is mutually agreeable. The monitor will document the date and time of all visits on a monitoring log that will be stored in the study regulatory binder.

During the visits, the site manager or investigator will provide the monitor with workspace and access to site facilities, source documents, and research records. The site manager or investigator will also be available to meet with the monitor to discuss findings and reply to inquiries.

After the visit, the monitor will produce a report to document all findings, discussions, and solutions. The report or a follow-up letter summarizing the contents of the report will be sent to the PI, the coordinating center, and the site manager. Additional follow-up may be conducted by email and telephone as needed.

10.2 Reporting of Unanticipated Problems, Adverse Events and Protocol Deviations

The PI will be responsible for ensuring that unanticipated problems (UPs), Adverse Events (AEs), and deviations are detected, documented, and reported in accordance with the protocol, NIEHS IRB policies, applicable SOPs (e.g., NIH HRPP SOP 16 "Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations"), and federal regulations. Recording and reporting of Adverse Events are described below within Section 10.3.

Serious unanticipated problems and serious protocol deviations will be reported to the IRB and CD as soon as possible and in writing on the Problem Report Form not more than 7 days after the PI first learns of the event. Not serious unanticipated problems and not serious deviations will be reported to the IRB and CD as soon as possible and in writing on the Problem Report Form not more than 14 days after the PI first learns of the event.

Deaths will be reported to the Clinical Director within 7 days after the PI first learns of the event.

All adverse events, deviations, and unanticipated problems will be summarized and reported at the time of Continuing Review.

10.3 Adverse Events

Adverse events associated with the study procedures are expected to occur very infrequently. Most of the risks associated with study procedures are mild, causing only transient discomfort.

10.3.1 Definition of an Adverse Event (AE)

Generally, an AE is defined as any unanticipated or unintended medical occurrence or worsening of signs, symptoms, or disease that occurs in a study participant after the time informed consent is obtained, regardless of the causal relationship of the event to study procedures. For the purposes of this study, signs and symptoms of pre-existing conditions that occur during the study will not be recorded as AEs, unless they are exacerbated by study procedures (based on the investigator's medical judgment). Additionally, medical events that occur outside the protocol-defined surveillance period (see Section 10.3.3) will not be recorded as AEs.

10.3.2 Definition of a Serious Adverse Event

A Serious Adverse Event (SAE) is defined as an AE occurring during the protocol-defined surveillance period (see Section 10.3.3) resulting in one of the following outcomes:

- Death
- Life-threatening event (defined as a condition that places a participant at immediate risk of death)
- In-patient hospitalization or prolongation of an existing hospitalization
- Persistent/significant disability or incapacity
- Medically important event that jeopardizes the participant and requires intervention to prevent one of the outcomes listed above

10.3.3 Adverse Event Surveillance Period

Surveillance for AEs will include the time period from when informed consent is obtained at the registry visit until completion of the visit. At the end of each visit, participants will be asked if they experienced any problems during the visit. Participants will also be instructed to contact the study staff if they experience any new problem within two days of a visit.

10.3.4 Reporting of Adverse Events

Only clinically significant adverse events (based on the investigator's medical judgment) will be reported to the IRB. Examples of clinically significant adverse events include:

- Fainting during spirometry or blood collection
- Respiratory distress induced by spirometry that requires medical attention
- Prolonged bleeding, hematoma formation, or infection associated with blood collection that requires medical attention

Field staff will be trained to detect and respond to clinically significant adverse events, and will be expected to report clinically significant adverse events to the coordinating center immediately.

At the time of the continuing IRB review, the PI will provide an aggregate summary of all clinically significant AEs.

Given the minimal risk of the procedures contained in the protocol, we anticipate SAE's to be very infrequent and therefore should be reported regardless of cause or association with preexisting conditions. The PI will report SAEs to the NIEHS IRB and NIEHS Clinical Director as soon as possible, but not more than 7 days after the PI first learns of the event.

10.3.5 Documenting Adverse Events

All AEs that are identified according to the definition provided in Section 10.3.1 will be entered onto a paper case report form (CRFs) or eCRFs, as applicable. The medical diagnosis of the event, time of onset, time of resolution or stabilization, the severity of the event, the investigator's judgment of the AE's relationship to the procedure, the expectedness of the event, action taken (if any), and outcome will also be recorded on the CRF. The CRF will be updated to reflect any changes in the status of the event that are recorded in source documents.

10.3.6 Management of Adverse Events

Any participant reporting an AE/SAE will be evaluated and managed appropriately by study staff. This could include immediate management at the study site, facilitation of emergency care, or referral to a primary care physician, public health clinic, or specialist.

The study staff will be responsible for ensuring appropriate follow-up care until the event resolves or stabilizes, and no more follow-up is required.

11 Data/Records Management

11.1 Data Management Responsibilities

The project team will be responsible for overseeing the collection of data into an in-house, secure electronic data management system and ensuring data accuracy, completeness, consistency, and timeliness. The investigator, study staff, coordinating center data manager, or contracted data manager will assist with the data management efforts.

Primary and final analyzed data will have study identifiers assigned so that research data can be attributed and linked to individual human subject participants, to be potentially combined with later research efforts. Appropriate security controls will be implemented to ensure that all data access is defined by roles, which restrict access to the bare minimum necessary for individuals to complete their project duties. All data management staff will receive data management system training as well as other relevant NIH training.

The investigator is ultimately responsible for assuring that data are complete, accurate, and recorded in a timely manner.

11.2 Data Capture Methods

Remote study computers or other electronic devices with whole-disk encryption will be issued to deployed research teams. A Data Management System (DMS) using a client-server architecture will be configured to standardize data collection and transmit data from remote devices to a centralized SQL database. The system will be accessible only to project team members at the coordinating center and NIH, via encrypted, secure connection SSS central servers (VPN or

Secure-Socket-Layer). Data collected on remote devices will typically be uploaded immediately. However, in cases where internet connectivity is not achievable, data will be encrypted and stored locally until such time a connection can be re-established (typically nightly). The system has user access rights designed to ensure site personnel have access only to participants assigned to their site, and cannot see data collected elsewhere.

Any ancillary data collected using third-party software will not contain PII when possible. All data management systems will be programmed in order to minimize the risk of errors. For example, real-time data validation and consistency checks will be performed as data is being collected, in order to preserve the integrity of the data. Study computers will be returned to the central office and appropriate agencies/organizations at the closure of data collection efforts.

In rare cases, the use of paper data collection materials may be required. The paper copies will be maintained as source documents and staff at the coordinating center will be responsible for ensuring proper transfer of the collected data to an electronic format.

The database server will be configured for 24/7 operation, and provide the capability of offsite backups. All relevant security planning will comply with the Federal Information Security Management Act of 2002 (FISMA), to ensure confidentiality, integrity and availability of the data and the DMS.

11.3 Types of Data

Data collected during the course of this study may include demography, anthropometry, spirometry, overall/general health information (including mental health), lifestyle, behavioral, residential, socioeconomic information and biospecimens (blood, urine, hair, buccal cell, saliva and nails) of participants.

11.4 Source Documents and Access to Source Data/Documents

Source documentation (the point of initial recording of information) should support the data collected and will be maintained to allow for the reconstruction and evaluation of the study. Source documents for this study will include original records and data, signed informed consent forms, completed questionnaires, and paper data collection worksheets utilized by study staff.

The Principal Investigator and study staff will ensure that all records, including source documents and regulatory documents pertaining to the conduct of this study, are made available to the NIEHS and its representatives and auditors from regulatory authorities to facilitate monitoring visits and/or study audits.

11.5 Study Records Retention

All study records will be retained indefinitely. Study records that will be retained include IRB approvals and correspondence, signed informed consent forms, tracking logs, contact information update forms, and other study documentation that may be developed during the course of the study. To protect against

accidental or premature destruction of these documents, the records will be maintained in a secure, locked storage areas that are only accessible to study staff.

All study data will be housed in a single data repository. This single database ensures that all system users are accessing the same database; allows for greater control via role-based access privileges; provides a robust architecture to support backup, security, and disaster recovery; and provides the flexibility needed to change the data input mechanisms that could change during a potentially long study.

Any loss or unanticipated destruction of samples or data (for example, due to freezer malfunction) that meets the NIH Intramural Protocol Violation definition or results in a violation that compromises the scientific integrity of the data collected for the study will be reported to the NIEHS IRB.

11.6 Data Sharing

Given the public health importance of research on the health effects of disasters, data and biospecimens from the RAPIDD Study will be made available for research use by any interested and qualified investigator or organization, within the limits of providing appropriate protection of research participants and compliance with their informed consent. Policies for data access will build on NIH established policies for controlled access to individual-level data in genome-wide association studies, as described at http://grants.nih.gov/grants/gwas/and open-access data sharing policies developed for other NIH sponsored longitudinal studies. In recognition of the rights and intellectual contributions of the RAPIDD investigators to publish data within a reasonable timeframe, outside researchers will also agree to include RAPIDD investigators as co-authors in their papers. Aggregate and summary data will be made publicly available along with information on all data that have been or will be collected. In order to prevent accidental disclosure of individual participant data, de-identified datasets are separately provided to qualified requesters; individual level data are not posted online. Access to the data will be granted by an NIH Data Access Committee which will ensure that these conditions are met initially and monitor subsequent compliance during the study.

11.7 Registration and User Agreements

Prior to the release of any study datasets, all users must complete a registration process. Any user requesting access to RAPIDD Study data must complete and sign a Data/Material User Agreement and a Data Transfer Agreement (DTA). Researchers will agree to keep the data secure, use the data only for approved research purposes, to not share the data with unauthorized users and not to attempt to identify individual study participants. Data recipients must also agree to destroy the data or return it to RAPIDD Study investigators when their work is complete. Additional proof of IRB approval or IRB exemption at one's home

institution will be required, to assure compliance with standards that assure the protection of participants' privacy and rights.

11.8 Biospecimens Access and Use of Cohort for Add-on Studies

Additionally, other investigators (both at NIH and outside) may wish to study the stored biospecimens or propose add-on studies that generate new data and/or involve direct participant contact. In that case, NIEHS IRB approval must be sought prior to any sharing of samples. Any clinical information shared about the sample would similarly require prior NIEHS IRB approval. Procedures and guidelines for proposing new assays or add-on studies will be established and posted. An independent committee will be established to review proposals for scientific merit, feasibility, and impact on the study cohort. The allocation of biospecimens will be assessed by the committee and rationing of samples may be implemented to minimize the depletion of biological samples. All recipients of RAPIDD biospecimens must complete a human material transfer agreement (MTA) prior to obtaining access to repository specimens.

12 Compensation

For their time and effort, participants will be reimbursed depending on the number and type of samples collected. Compensation will be $35 for the blood draw, $15 for the urine sample, $10 for the sample of saliva, buccal cells, or hair, $20 for spirometry, and $20 for providing nail clippings. Payment will be provided by gift card upon completion of each visit.

13 Study Termination

This study may be terminated at any time either by the Investigator, the NIEHS IRB, or NIEHS leadership, provided there is reasonable cause and sufficient notice is given in advance of the intended termination. Reasons for such action include, but are not limited to:

- Inadequate recruitment of participants
- Failure of the investigator to comply with the protocol
- Failure of the PI to comply with IRB Continuing Review policies
- Safety concerns
- Successful completion of the study

If a decision is made to terminate the study, the investigator will submit a plan for study termination and submit it to the IRB within 30 days of the notice of termination.

14 Scientific References

1. Lurie N, Manolio T, Patterson AP, Collins F, Frieden T. Research as a part of public health emergency response. N Engl J Med. 2013 Mar 28;368(13):1251–5.
2. Sorbello, A., S. C. Jones, et al. (2012). "Emergency use authorization for intravenous peramivir: evaluation of safety in the treatment of hospitalized patients infected with 2009 H1N1 influenza A virus." Clin Infect Dis 55(1): 1-7.
3. Institute of Medicine (US). Assessing the Effects of the Gulf of Mexico Oil Spill on Human Health: A Summary of the June 2010 Workshop. Washington (DC): National Academies Press (US); 2010. Available from: http://www.iom.edu/Reports/2010/Assessing-the-Effects-of-the-Gulf-of-Mexico-Oil-Spill-on-Human-Health.aspx.
4. National Biodefense Science Board (NBSB). Call to Action: Include Scientific Investigations as an Integral Component of Disaster Planning and Response [Internet]. Department of Health and Human Services; 2011 Apr. Available from: http://www.phe.gov/Preparedness/legal/boards/nprsb/Documents/nbsbrec14.
5. Institute of Medicine (US). Enabling Rapid and Sustainable Public Health Research During Disasters: Summary of a Joint Workshop by the Institute of Medicine and the U.S. Department of Health and Human Services: National Academies Press; 2014. Available from: http://www.nap.edu/catalog/18967/enabling-rapid-and-sustainable-public-health-research-during-disasters-summary
6. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005;26(2):319 –338.
7. Miller MR, Crapo R, Hankinson J, Brusasco V, Burgos F, Casaburi R, et al. General considerations for lung function testing. Eur Respir J. 2005 Jul 1;26(1):153 –161.
8. Buist AS, McBurnie MA, Vollmer WM, Gillespie S, Burney P, Mannino DM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet. 2007 Sep 1;370(9589):741–50.
9. Menezes AMB, Perez-Padilla R, Jardim JRB, Muiño A, Lopez MV, Valdivia G, et al. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. Lancet. 2005 Nov 26;366(9500):1875–81.

Appendix A: List of Appendices

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Appendix B: Protocol Amendment Checklist

This checklist is designed to streamline the process of IRB review prior to study initiation. Based on the type of disaster, this checklist will provide specific details of study setting, target sample size, procedures and questionnaires that will be administered, as well as exposures and potential health effects of interest. This checklist also provides information about modified study documents (i.e., ICF revisions, additional questionnaires, etc.). Appendix D provides an example scenario where this checklist would be submitted for IRB approval prior to study initiation for a specific disaster.

I. Type of Disaster

Natural Disasters	***Man-made and Technological Disasters***
☐Earthquake/Tsunami	☐Chemical release/Oil spill
☐Flood	☐Biological emergency
☐Hurricane	☐Radiological/Nuclear
☐Tornado	☐Explosion
☐Wildfire	☐Civil unrest/ war
☐Extreme Temperature/Drought	☐Utility service disruption/blackout

☐Other: _____

II. Detailed description of disaster and justification for deployment:

_____
_____
_____
_____
_____

III. Research Setting:

_____

IV. Estimated Sample Size: _____

V. Accrual duration: _____

VI. Procedures:

☐ Core Biospecimen Set

- Urine Collection
- Oragene or buccal cell collection

☐ Basic Biospecimen Set

- Vital Signs
- Anthropometry
- Pulse Oximetry
- Venipuncture

- Urine Collection

☐ Enhanced Biospecimen Set

- Vital Signs
- Pulse Oximetry
- Urine Collection
- Nail Clipping Collection
- Hair Collection
- Anthropometry
- Venipuncture
- Spirometry
- Oral Swab Saliva Collection

☐Additional procedures: _____

☐Vital signs
☐Pulse Oximetry
☐Anthropometry
☐Venipuncture
☐Urine collection
☐Spirometry
☐Nail clipping collection
☐Oral swab saliva collection
☐Oragene or buccal cell collection
☐Hair collection

(Provide description of procedure and list document changes and section numbers in section X of this sheet.)

VII. Questionnaires (check all that will be completed during the visit):

☐ Core Registry Form
☐ Basic Health Registry Form
☐ Enhanced Health Registry Form
☐Other: _____

(A detailed list of the actual questionnaires to be used can be found in attachment [##] in section X of this sheet.)

VIII. Outcomes of interest:

☐Cardiovascular System
☐Digestive System
☐Endocrine System
☐Excretory System
☐Immune System
☐Integumentary System
☐Muscular System
☐Nervous System
☐Reproductive System
☐Respiratory System
☐Skeletal System
☐Other
_____

IX. Provide a description of protocol, consent, and/or other document changes with section numbers.

X. List of attachments:

Appendix C: Questionnaires Available for RAPIDD

Based on the type of disaster, research question of interest, available time, feasibility of administration and operations on the ground, the appropriate Registry Form and/or Biological Specimen Questionnaire can be selected for use. The Core Registry Form can be administered to collect contact information and complete rostering if time and resources are severely limited. All of the mental health questions included in the Basic and Enhanced Health Registry Forms have been previously reviewed by the NIEHS IRB as components of the NIEHS GuLF Study. In addition to the questionnaires included in Appendix C, tools and resources can be located in DisasterLit at the National Library of Medicine's Disaster Information Management Research Center[1].

Questionnaire & Brief Description **Interviewer Administered Registry Forms – Use ONLY ONE**	**# of Questions**
Core Registry Form: Registry and Contact information - Modified from ATSDR Rapid Registry Form	27
Basic Health Registry Form: Registry and Contact information - Modified from ATSDR Rapid Registry Form Demographics and Sociological Factors - Sources: Emergency Responder Health Monitoring and Surveillance (ERHMS), NHANES (2011, 2013-2014), Environmental Protection Agency National Human Exposure Assessment Survey (EPA NHEXAS) General Health - Source ERHMS Mental Health - Source PHQ-2, GAD-2, PC-PTSD Deployment Information - Source ERHMS, ATSDR Rapid Registry Form, Department of Defense (DOD) / Department of Homeland Security Post Deployment Form Pre-Deployment Information - Modified from ATSDR Rapid Registry Form Pre-Deployment Exposures and Past History Exposures - Source ERHMS Post-Deployment Information - Modified from ATSDR Rapid Registry Form Post-Deployment Exposure Information - Source ATSDR Rapid Registry Form	81
Enhanced Health Registry Form: Registry and Contact information - Modified from ATSDR Rapid Registry Form Demographics and Sociological Factors - Sources: PhenX toolkit, NHANES, EPA NHEXAS General Health – Sources: ERHMS, Department of Defense, ACE Health Survey module F Mental Health – Sources: PHQ-9, GAD-7, PCL-S Pre-Deployment Information - Modified from ATSDR Rapid Registry Form Pre-Deployment Exposures and Past History of Exposure – Source: EHRMS Post-Deployment Information - Modified from ATSDR Rapid Registry Form Post-Deployment Exposure Information – Source: ATSDR Rapid Registry Form	148

[1] There are over 150 data collection instruments available within DisasterLit (http://disasterlit.nlm.nih.gov/) Each tool listed in DisasterLit has metadata (e.g., number of items, ease of use in a disaster setting, how it is administered, populations in which it has been used, translated versions, existence of validation/reliability studies) associated with it to help guide decisions about its use.

Biospecimen Collection	
Core Biospecimen Collection Urine and Oragene or buccal cell collection with option for self-collection on site	27
Basic Biospecimen Collection Interviewer administered questionnaire about the collection of biological specimens. • Vital Signs • Pulse Oximetry • Urine Collection • Anthropometry • Venipuncture	34
Enhanced Biospecimen Collection Interviewer administered questionnaire about the collection of biological specimens. • Vital Signs • Pulse Oximetry • Urine Collection • Nail Clipping Collection • Hair Collection • Anthropometry • Venipuncture • Spirometry • Oral Swab Saliva Collection	66

Appendix D: Example of Protocol Implementation During a Disaster Scenario

Hurricane Scenario

A Category 5 Hurricane (highest category on the Saffir-Simpson Hurricane Scale) has made landfall in Wilmington, North Carolina resulting in catastrophic damage to the Cape Fear region. Maximum sustained winds were greater than 160 mph and the storm surge exceeded 20 feet. Many structures in the region have been destroyed and there is a large amount of debris on the streets. Floodwaters in low-lying areas have not receded and it is suspected that they are tainted with raw sewage, pesticides, animal, agricultural waste and other environmental contaminants. Though massive evacuations saved many lives, residents who failed to evacuate in a timely fashion were left stranded resulting in a significant search and rescue operation. A FEMA urban search and rescue task force and incident support team based in Washington, D.C. has been activated to respond to the region. Additional groups of local/state disaster workers and volunteers are deploying to the region to assist in rapid needs assessment and cleanup operations.

The needs of the local community have exceeded the resources available to local/regional authorities and there has been an official request from the City of Wilmington for state and federal assistance. The concern about exposure to hazardous materials in the post-hurricane environment has led NIEHS to consider implementation of the RAPIDD protocol. A large cadre of local disaster workers who have received Hazardous Waste Worker Training under the NIEHS Worker Training Program (WTP) are preparing to deploy to the region. NIEHS has identified this disaster worker group as a cohort of interest to determine the health impact of the hurricane on responders. Since the RAPIDD protocol has already received IRB pre-approval to study a disaster responder cohort, the implementation of the study can be expedited to permit the collection of baseline data from the WTP trained disaster worker group prior to exposure to possible hazardous materials in the post-hurricane environment. The RAPIDD study team submits the Protocol Amendment Checklist (Appendix B) and requests an expedited review of the RAPIDD protocol. Since the NIEHS IRB has already pre-approved the body of the RAPIDD protocol, the IRB can solely review the new material which should reduce the time needed for an approved protocol to be initiated in the field. Once approval is attained, a pre-designated and trained corps of “research responders” is activated by NIEHS to implement the RAPIDD Study and is deployed to the pre-deployment staging area in Wilmington. A sample completed Appendix B checklist for this disaster scenario is provided below.

Sample Completed Protocol Amendment Checklist

I. Type of Disaster

Natural Disasters	***Man-made and Technological Disasters***
☐Earthquake/Tsunami	☐Chemical release/Oil spill
☐Flood	☐Biological emergency
☒Hurricane	☐Radiological/Nuclear
☐Tornado	☐Explosion
☐Wildfire	☐Civil unrest/ war
☐Extreme Temperature/Drought	☐Utility service disruption/blackout

☐Other: _____

II. Detailed description of disaster and justification for deployment:

The City of Wilmington has requested support from state and federal resources and the NIEHS Worker Training Program (WTP) responders have been deployed to the Cape Fear region to respond to Hurricane X. There is concern over the environmental contaminants in the floodwaters (e.g., raw sewage, pesticides, animal, agricultural waste) and the effects of exposure to these hazardous substances. Rapid collection of baseline data from WTP disaster responders will be valuable in investigating the potential short- and long-term health effects of exposure to the debris and flood waters following this hurricane.

III. Research Setting: WTP Staging Area in Wilmington, NC_____

IV. Estimated Sample Size: 100_____

V. Accrual duration: 2 months_____

VI. Procedures:

☐ Core Biospecimen Set

- Urine Collection
- Oragene or buccal cell collection

☒ Basic Biospecimen Set

- Vital Signs
- Pulse Oximetry
- Urine Collection
- Anthropometry
- Venipuncture

☐ Enhanced Biospecimen Set

- Vital Signs
- Pulse Oximetry
- Anthropometry
- Venipuncture

- Urine Collection
- Nail Clipping Collection
- Hair Collection
- Spirometry
- Oral Swab Saliva Collection

☐Additional procedures: _____

☐Vital signs
☐Pulse Oximetry
☐Anthropometry
☐Venipuncture
☐Urine collection
☐Spirometry
☐Nail clipping collection
☐Oral swab saliva collection
☐Oragene or buccal cell collection
☐Hair collection

(Provide description of procedure and list document changes and section numbers in section X of this sheet.)

VII. Questionnaires (check all that will be completed during the visit):

☐Core Registry Form
☒Basic Health Registry Form
☐Enhanced Health Registry Form
☐Other: _____

(A detailed list of the actual questionnaires to be used can be found in attachment [##] in section X of this sheet.)

VIII. Outcomes of interest:

☒Cardiovascular System
☒Digestive System
☐Endocrine System
☐Excretory System
☐Immune System
☐Integumentary System
☐Muscular System
☐Nervous System
☐Reproductive System
☒Respiratory System
☐Skeletal System
☐Other _____

IX. Provide a description of protocol, consent, and/or other document changes with section numbers.

Protocol – No changes have been made to the protocol

ICF –

1. Inserted disaster name – pg. 1 “What is the purpose of this study?”
2. Listed study procedures – pg. 2 “What will I be asked to do in this study?”
3. Inserted estimated time of enrollment and study exam – pg. 3 “ How long will the study procedures take?”
4. Revised remuneration amounts based on procedures specific to this disaster – pg. 4 “Will I be paid for participating?”

ICF quick reference guide –

1. Listed study procedures – “During the registry visit”
2. Revised remuneration amounts – “Payment to Participants”

FAQs –

1. Listed study procedures – “What will I be asked to do”
2. Revised remuneration amounts – “Will I receive compensation for participating in this study?”

Basic Health Registry Questionnaire –

1. Inserted disaster name – pg. 1 script
2. Inserted estimated time for completion – pg. 1 script

X. List of attachments:

Existing or revised documents

- ICF
- ICF quick reference guide
- FAQs
- Basic Health Registry Questionnaire
- Medical results handouts

New documents

- Recruitment script
- Informational study handout
- Medical referral handout
- Certificate of Confidentiality

Appendix E: Medical Referral Values and Recommended Actions

Evaluation	Findings	Recommended Actions
Blood Pressure	SBP ≥ 180 or DBP ≥ 110	Seek care **as soon as possible** as this is a potential emergency health condition. **Based on AHA 2010 guidelines*
	SBP 160 to 179 or DBP 100 to 109	See a health care provider **within the next month.**
	SBP 140 to 159 or DBP 90 to 99	See a health care provider **within the next two months.**
	SBP 120 to 139 or DBP 80 to 89	Find out from a health care provider if any additional evaluations or lifestyle changes are indicated.
	SBP < 120 AND DPB < 80	No recommendation.
Resting Heart Rate	HR > 120 bpm	See a health care provider **as soon as possible**.
	101 ≤ HR ≤ 120 bpm	See a health care provider **within the next month**.
	40 ≤ HR ≤ 59 bpm	Participant may want to discuss findings with their health care provider.
	HR < 40 bpm	See a health care provider **as soon as possible**.
	60 ≤ HR ≤ 100	No recommendation.
BMI	Obese (≥ 30)	If obese, overweight, or underweight, discuss results and potential lifestyle changes with a health care provider.
	Overweight (25 to 29.9)	
	Normal (18.6 to 24.9)	
	Underweight (< 18.5)	
Spirometry	Either FEV_1, FVC, or FEV1/FVC below lower limits of normal AND FEV_1, < 50% predicted	See a health care provider **within the next week**.
	Either FEV_1, FVC, or FEV1/FVC below lower limits of normal AND FEV_1, ≥ 50% predicted	See a health care provider **within the next month**.

Evaluation	Findings	Recommended Actions
	FEV_1, FVC, and FEV1/FVC all above lower limits of normal	No recommendation.
Pulse Oximetry	SpO2 between 95%-100% - considered normal range	No recommendation.
	SpO2 between 91% - 94% - suggests hypoxemia or other health problem may be present	Participant is advised to discuss findings with their health care provider.
	SpO2 < 90% - suggest possible acute respiratory failure	Seek care **as soon as possible** as this is a potential emergency health condition.

Appendix F: Review of RAPIDD Protocol Implementation

The purpose of this worksheet is to evaluate the implementation of the RAPIDD protocol to ensure that the safeguards put in place at the time of original approval are adequate to protect the safety of actual subjects in the specific disaster setting. Based on the type of disaster, this worksheet will provide summary details about enrollment, response rates, adverse events, any new information that may affect risk or benefit to participants, and evaluation of study procedures. This completed worksheet must be submitted to the NIEHS Institutional Review Board **within 60 days** of study protocol implementation. A template outline for the RAPIDD protocol implementation review report is as follows:

I. Description of study progress (provide a narrative describing the disaster and its impact, the deployment setting, operational environment, etc.):

II. Evaluation of recruitment and enrollment (provide information about recruitment methods, response rates, subject accrual demographics, summary statistics on enrolled subjects, and evaluation of the enrollment location):

III. Evaluation of study procedures (provide information about the effectiveness of study operations, studyprocedures, and whether or not procedures interfered with disaster worker responsibilities):

IV. Discussion of any new information that may affect risk or benefit to subjects:

V. Summary of adverse events and any unanticipated problems involving risks to subjects or others:

VI. Explanation of how this research could benefit the community or our understanding of the community impacts:

VII. Description of data and safety monitoring plan:

VIII. List of collaborators and their contributions to success/failure:

IX. Justification for continued study of enrolled participants based on cumulative results thus far, including new interesting specific endpoints of the study:

X. Suggested protocol modifications, if applicable: