Human Health Exposure Analysis Resource (HHEAR)
Initial Application for HHEAR Services - EXAMPLE

Application Template: This document is provided for informational purposes only.
All HHEAR Applications must be submitted on-line at: myhhear.hhearprogram.org.
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Step 1 of 9: Background/Introduction

The HHEAR Application is for investigators who wish to apply for HHEAR laboratory and data analysis services to add or broaden analyses of environmental exposures in their studies of human health.

Before submitting an Initial Application, please review the policies and procedures for accessing HHEAR services.

Contact HHEARhelp@westat.com with any questions about this Application.

Instructions

- Step 1: Review background/introduction.
- Step 2: Complete the section on investigator eligibility. If you have questions about your eligibility, contact HHEARhelp@westat.com.
- Step 3: Review HHEAR policies and indicate your agreement.
- Step 4: Specify which HHEAR services you are requesting.
- Step 5: Provide information about yourself, a project contact person, and any co-investigators.
    - If you do not have the authority to commit to the transfer of biological and/or environmental specimens and data, list contact information for those who do.
    - Upload biographical sketches for yourself and co-investigators. Use the standard NIH biographical sketch format PHS 398.
- Step 6: Provide information on your parent study.
    - Provide succinct responses to each item. Note word/character limits.
- Step 7: Provide information about your proposed HHEAR project.
    - Provide succinct responses to each item. Note word/character limits.
    - Upload a list of citations of key references that provide scientific premise for the proposed project including the rationale for requested services.
- Step 8: Preview application.
- Step 9: Complete application.

Step 2 of 9: Investigator Eligibility

Please provide responses to each item below to indicate your eligibility for HHEAR services.

You have an ongoing or completed epidemiological or clinical study with human biological and/or environmental samples linked to health outcome data.

☐ Yes ☐ No

You want to add environmental exposure data to your study or need more extensive analysis of exposures to support your scientific hypothesis related to health outcomes.

☐ Yes ☐ No

Although your parent study may be ongoing, you have collected all data, biological and environmental samples that will be provided to HHEAR for the proposed project prior to submitting your final application.

☐ Yes ☐ No

You meet at least one of the following funding criteria.

☐ Yes ☐ No

- Your study is funded at least in part by NIEHS extramural funds. Studies funded by NIEHS extramural funds are eligible for targeted and untargeted analysis of biological and environmental samples.
- Your study is currently funded by the NIEHS Superfund Research Program. Studies funded by the NIEHS Superfund Research Program are eligible for targeted and untargeted analysis of environmental samples, and only untargeted analysis of biological samples.
- Your study is currently funded at least in part by NHLBI extramural funds. Studies funded by NHLBI extramural funds are eligible for targeted and untargeted analysis of only biological samples.
- Your study is currently funded by NCI extramural funds and has more than one year of funding remaining at the time you submit the HHEAR initial application. Studies funded by NCI extramural funds are eligible for only targeted analysis of biological samples.
- Your study is an ECHO-wide cohort analysis proposal that has been approved through the ECHO Publications Program, or an ECHO Opportunities and Infrastructure Fund (OIF) proposal approved through the ECHO OIF Program. Studies funded by ECHO are eligible for targeted and untargeted analysis of only biological samples.
    - ECHO-wide and OIF supported projects are managed through the ECHO program and do not require an additional application for HHEAR services.

ECHO cohorts may be eligible for cohort specific analyses through NIEHS, NHLBI, or NCI support through a HHEAR application.

- Email echocc-publications@dm.duke.edu for more information on the ECHO Publications Program. Email echocc-oif@duke.edu for more information on the ECHO OIF Program.

You are eligible to apply for an NIH grant at your home institution, with authority to commit to documentation such as the Material Transfer Agreement, Data Submission Agreement, and Data Sharing Plan

☐ Yes ☐ No

You agree to share experimental design details and supporting data, including phenotypic data at the individual level, needed to achieve the aim(s) of your proposal?

☐ Yes ☐ No

Step 3 of 9: Agreement to HHEAR Policies

Please indicate that you have read and will comply with the Policies for Access to HHEAR Services by adding your eSignature in the space provided.

I have read and will comply with the HHEAR policies for accessing services.

☐ Yes ☐ No

eSignature

If no, please provide an explanation:

(100 words remaining)

Are you subject to any other data sharing policies (e.g., a consortium agreement that your data must adhere to)?

☐ Yes ☐ No

If yes, please provide an explanation:

(100 words remaining)

Step 4 of 9: Request HHEAR Services

Please indicate the HHEAR services you are requesting (select all that apply):

- ☐ Laboratory analysis of biological samples
- ☐ Laboratory analysis of environmental samples
- ☐ Statistical analysis

Step 5 of 9: Applicant/Investigator Information

Project number:

Principal Investigator: *Principal Investigator (PI) contact information has been prefilled from your myHHEAR account registration information. Indicate whether the PI has the authority to commit to the transfer of samples and/or data.*

Name:

Institution:

Phone:

Email:

Biosketch:

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Cohort name:

Website link (if available):

Authority to commit to transfer

Biological Samples: ☐ Yes ☐ No ☐ N/A

Environmental Samples: ☐ Yes ☐ No ☐ N/A

Data: ☐ Yes ☐ No

Other Investigator: *Complete this item for the investigator with the authority to commit to transfer of biological/environmental samples and/or data, if it is not the PI. If you propose to use samples and/or data from more than one cohort, click the "Add Other Investigator(s)" button below to provide this information for all biological/environmental samples and data sources.*

Name:

Institution:

Phone:

Email:

Role: ☐ **Co-Investigator**

☐ **Other (specify):**

Biosketch:

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Cohort name:

Website link (if available):

Authority to commit to transfer

Biological Samples:	☐ Yes	☐ No	☐ N/A
Environmental Samples:	☐ Yes	☐ No	☐ N/A
Data:	☐ Yes	☐ No	

ADD OTHER INVESTIGATOR(S)

Project Contact Person (if different from Principal Investigator):

Name:

Institution:

Phone:

Email:

Step 6 of 9: Parent Study Information

*Please complete each item below to provide the key information that can be used by reviewers to understand the **parent study** for the proposed project. If there is more than one parent study providing data and biological and/or environmental samples, provide the information for each parent study. Do not leave any items blank.*

1. Parent study project title:

2. Parent study cohort information:

Cohort name:

Cohort website link (if available):

3. Parent study funding source(s):

4. Parent study Principal Investigator and institution:

5. Parent study key publications *(limit to 3; provide as PMIDs)*:

6. Primary hypothesis of the parent study:

(20 words remaining)

7. Summary of main published findings for parent study:

(100 words remaining)

8. Parent study design: *(Check all that apply)*

☐ Cross-sectional ☐ Hospital-based ☐ Ambispective cohort

☐ Case-control ☐ Prospective cohort ☐ Intervention study

☐ Population-based ☐ Retrospective cohort ☐ Clinical trial

☐ Other: (specify)

9. Parent study population description:

(80 words remaining)

a. Sample size for parent study* (e.g., # cases and controls if case-control study, number of cohort members if cohort study):

**If study is longitudinal, please indicate the sample size at the first time point as well as the last time point.*

b. Age range(s) of parent study population (at study entry):

c. Has the parent study population been included in a previous CHEAR/HHEAR project or in a previous ECHO project?

☐ Yes ☐ No

d. Geographic location(s) of the parent study population:

e. Years in which the parent study was conducted:

f. Method of data collection (e.g., survey, in-person visits, medical records) for the parent study:

g. Number of data collection time points and interval between data collection time points for the parent study:

10. Main exposures (environmental and/or non-environmental) investigated for the parent study:

11. Type of biological and/or environmental samples collected (i.e., whole blood, plasma, urine) for the parent study:

a. Years in which biological samples were collected for the parent study:

b. Number of samples collected per study participant/interval between sample collection for the parent study:

c. Years in which environmental samples were collected for the parent study:

Step 7 of 9: Proposed HHEAR Project

Please complete each item below to provide the key information that can be used by reviewers to evaluate your proposed project.

Proposed Project Title:

1. Abstract:

*Please provide a summary (hypotheses, study design, methods and statistical analysis) of your **proposed HHEAR project** in the context of the parent study.*

(150 words remaining)

2. Specific aim(s) for proposed HHEAR project:

a. Specific aim 1:

b. Specific aim 2 (if applicable):

c. Specific aim 3 (if applicable):

3. Exposures to be investigated for proposed project:

4. Significance:

a. Describe the scientific premise for the proposed HHEAR project including the rationale for requested services (targeted, untargeted, and/or environmental analysis). Please provide citations when applicable and indicate which are "key" references for the rationale:

(250 words maximum)

List of citations:

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b. Explain how the proposed project will improve scientific knowledge of the comprehensive effects of environmental exposures on human health noting advancements over previous research on this topic. Include any information related to life stage (e.g., infants, adolescents, adults, seniors) that the project may focus on:

(200 words maximum)

c. Describe how the requested HHEAR analyses will enhance the findings from the parent study:

(100 words maximum)

5. Study design of proposed HHEAR project:

(250 words maximum)

a. Study sample size:

b. Relationship between participants (if applicable) (e.g., mother–child, siblings, family based trios):

c. Provide, in a narrative, a breakdown of the total number of participants with biological and/or environmental samples available for analysis by visit and/or age:

Proposed Project Biological Sample Characteristics and Analyses: *Complete Table 1 to provide information on characteristics of participants, the associated biological samples that will be provided, and the requested laboratory analyses. Complete a separate row for each unique combination of characteristics. Provide the biological sample information in as much detail as possible. For example, if you are providing serial serum and urine samples collected from men and women at Time 1 and Time 2, you would complete 8 rows of the Table. If you have a sample matrix that does not match a specified option, select "O – Other" and specify the matrix in the Other Comments section. If you need to add rows to the table, contact HHEARhelp@westat.com.*

Table 1: Proposed Project Biological Sample Characteristics and Analyses

Priority Order for Analyses	**Laboratory Analyses (exposure measures)** *(select from drop down)*	**Participant Type** *(select from drop down)*	**Age/Stage at Collection** *(e.g., ages 0-2, first trimester)*	**Sample Matrix** *(select from drop down)*	**# Partici -pants**	**# Samples per Partici-pant**	**# Total Samples**	**Available Volume per Sample** *(with units)*	**Collection Method** *(e.g. morning void, fasting, passive drool)*	**Storage Temp** *(with units)*	**# of Freeze-Thaws**	**Sample Collection Status** *(All or Some)*
	SELECT ONE:	SELECT ONE:		SELECT ONE:								
ADD ROW												

Environmental Samples and Analyses. *Complete Table 2 to provide information on the environmental samples that will be provided to HHEAR and requested lab analyses. Complete a separate row for each unique combination of characteristics. Provide the environmental sample information in as much detail as possible. If you have a sample matrix that does not match a specified option, select "O – Other" and specify the matrix in the Other Comments section. If you need to add rows to the table, contact HHEARhelp@westat.com.*

Table 2: Proposed Project Environmental Sample Characteristics and Analyses

Priority Order for Analyses	**Laboratory Analyses** *(select from drop down)*	**Sample Matrix** *(select from drop down)*	**# Samples**	**Available Total Volume/ Quantity** *(with units)*	**Storage Temp** *(with units)*	**# of Freeze-Thaws**
	SELECT ONE:	SELECT ONE:				
ADD ROW						

6. Provide information on the collection method employed, including the tools and materials used to collect the environmental sample, and any sample processing that was conducted (e.g., sieving) and the containers used to store the samples. Please also include the location where the samples were collected (e.g., if dust, where in the house was the dust collected?):

(100 words maximum)

7. In the items below, provide information about the variables that will be submitted to HHEAR for data analysis:

a. Outcome(s): (Check all that apply)

- ☐ Asthma
- ☐ Autism
- ☐ Biomarker validation
- ☐ Blood disease
- ☐ Cancer
- ☐ Coronary heart disease
- ☐ Other:
- ☐ Cardiovascular risk/disease
- ☐ Chronic obstructive pulmonary disease
- ☐ Cystic fibrosis
- ☐ Diabetes
- ☐ Idiopathic pulmonary fibrosis
- ☐ Infectious disease
- ☐ Liver disease
- ☐ Neurologic/Cognitive development
- ☐ Obesity/Growth
- ☐ Pregnancy Outcomes
- ☐ Respiratory health
- ☐ Sleep apnea

b. Details on outcome assessment(s):

(50 words maximum)

c. List key covariates:

(50 words maximum)

d. Provide frequency tables of key covariates and outcomes (for both the proposed study and the parent study), including missing (by time point if applicable) as an attachment. If not currently possible, provide a description of expected missingness on all key covariates and outcomes. If you don't currently have access to this information, please explain why.

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8. Statistical analysis plan

a. Provide a summary description of the analysis strategy and statistical approaches proposed to address each aim. In your explanation, address the following points, as applicable (e.g., confounding, non-linearity, mixtures, combined effect of multiple exposures, potential interactions), and indicate how the proposed strategy will be evaluated to ensure validity, generalizability, and interpretability:

(*350 words maximum*)

b. Provide power calculations (e.g., measureable effect size, sample size calculations) for each aim or explain the rationale for why the anticipated sample size is sufficient:

(*100 words maximum)*

9. Challenges and biases that might be encountered in conducting the proposed study analysis:

(50 words maximum)

Step 8 of 9: Preview Application

Completed electronically

Step 9 of 9: Complete Application

Completed electronically

Additional Information

The following shows the drop-down options for each of the tables in the application.

Table 1 Drop-Down Options: Proposed Project Biological Sample Characteristics and Analyses

Laboratory Analyses (exposure measures)	BFR - Brominated Flame Retardants DNA Adducts DRUG - Pharmaceuticals and Drugs of Abuse INFLAM - Cytokines and Other Inflammatory Markers NUTRIENTS OPE - Organophosphate Ester Flame Retardants & Plasticizers OXID - Oxidative Stress PAH - Polycyclic Aromatic Hydrocarbons PESTICIDES (Current Use) PESTICIDES (Legacy) PFAS - Perfluoroalkyl and polyfluoroalkyl substances PHENOLS PHTHALATES SMOKE - Tobacco Metabolites STRESS (Cortisol) TARGET - Other Targeted Analysis TRACE ELEMENTS UNTARGETED VOC - Volatile Organic Compounds
Participant Type	Adults (18+ years) Adolescents (12-17 years) Children (1-11years) Infants (0-12 months) Pregnant Mothers
Sample Matrix	B - Whole Blood BLF - Bronchial Lavage Fluid BR - Breast Milk BT - Biopsied Tissue BU - Buccal Cell CB - Cord Blood CP - Cord Plasma CS - Cord Serum CSF - Cerebrospinal Fluid CT - Cord Tissue D - DNA DBS - Dried Blood Spots EBC - Exhaled Breath Condensate H - Hair

	ME - Meconium N - Nails O - Other OT - Other Tissue PC - Plasma Citrate PE - Plasma EDTA PH - Plasma Heparin PL - Placenta R - RNA RBC - Red Blood Cells S - Serum SL - Saliva ST - Stool T - Teeth U - Urine WBC - White Blood Cells

Table 2 Drop-Down Options: Proposed Project Environmental Sample Characteristics and Analyses

Laboratory Analyses (exposure measures)	BFR - Brominated Flame Retardants OPE - Organophosphate Ester Flame Retardants & Plasticizers PAH - Polycyclic Aromatic Hydrocarbons PESTICIDES (Current Use) PESTICIDES (Legacy) PFAS - Perfluoroalkyl and polyfluoroalkyl substances PHENOLS PHTHALATES TARGET - Other Targeted Analysis TRACE ELEMENTS UNTARGETED
Sample Matrix	AS - Air Samplers HD - House Dust HW - Hand Wipes SS - Soil/Sediment DW - Drinking Water SGW - Surface/Ground Water SW - Silicone Wristbands O - Other