

Site Training

MARC-43:

Airway microbiome and age 6-year
asthma phenotypes in
a healthy infant cohort



ECHO

Environmental influences
on Child Health Outcomes

A research program supported by the National Institutes of Health

Study Leadership

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**MARC-35/43
Steering Committee**

Outline of Presentation

1. Overview
2. Enrollment
3. Specimen Collection
4. Follow-up by Sites
5. REDCap

ECHO Program

Goal: to determine the factors that influence child health outcomes

Research focus areas:

1. Airway
2. Development
3. Obesity
4. Neurodevelopment
5. Child Health



ECHO

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ECHO Program (continued)

- ECHO will:
 - Pool data from existing cohorts (n~50,000 children) for analysis
 - Collect prospective data in standardized way from multiple cohorts
- Program infrastructure includes possibility of laboratory and data analysis support

CHIME Study

CHildhood MicrobiomE (CHIME) study



(draft logo)



ECHO

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MARC-43 Study Design

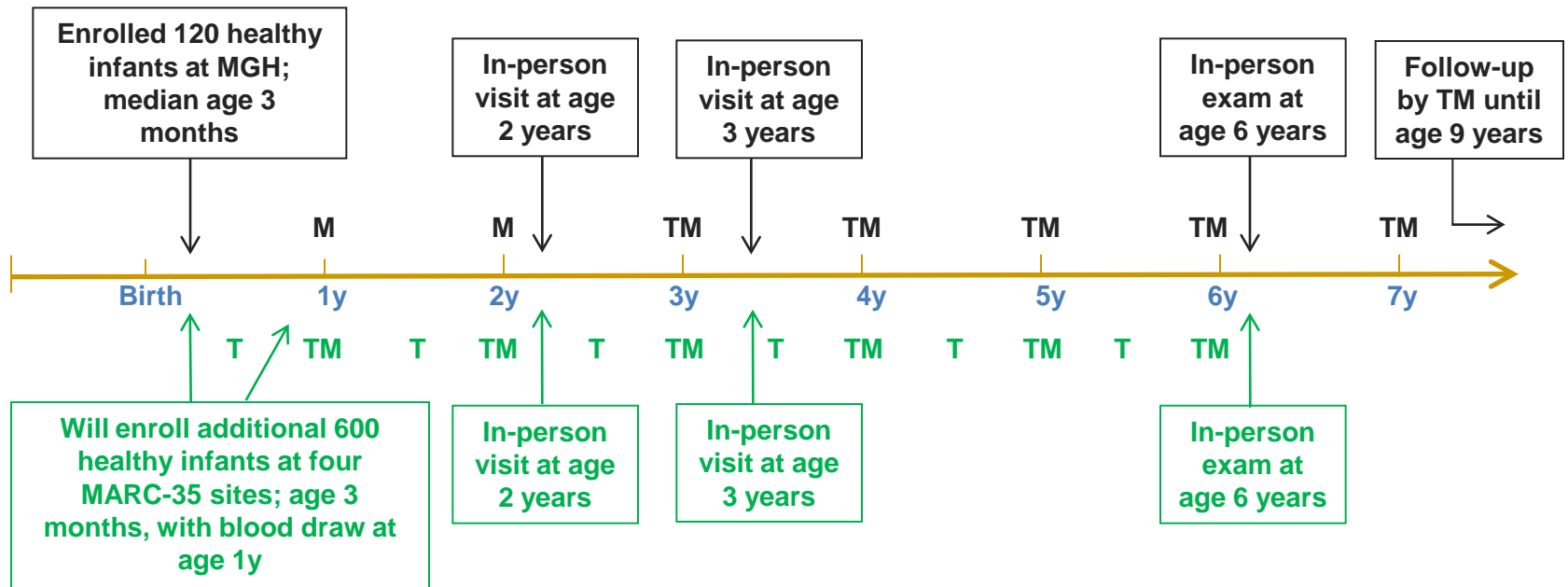


Figure. Overall study design, shown by child age (blue). Expansion of the original MGH Healthy Infant cohort (n=120) (black); newly enrolled 600 healthy infants from four sites (green). Abbreviations: T, telephone interview; M, medical records.

NOTE: All telephone follow-up interviews done by callers at the EMNet Coordinating Center.

ECHO Grant Aims

1. To investigate the relation of the airway microbiome to risk of childhood asthma among infants with severe bronchiolitis (MARC-35)
2. To investigate the relation of the airway microbiome to risk of childhood asthma among healthy infants (MARC-43)

ECHO Grant Aims (continued)

3. To investigate the relation of longitudinal patterns of the airway microbiome (e.g., infancy, age 3y, and age 6y) to the risk of childhood asthma in the MARC-35 and MARC-43 cohorts combined

Significance

- Emerging evidence that the airway microbiome influence immune responses in the airway, and that the airway microbiome may be an important risk factor for incident asthma. No prior studies have examined this question.
- The mechanistic link between the airway microbiome and asthma pathogenesis remains unclear.
- Despite asthma heterogeneity, no longitudinal studies have examined development of different asthma phenotypes in children.

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Inclusion Criteria

- Age 28 days – 11.99 months
- Presented to the participating site for a well-child visit or other clinical visit
- Parent speaks English or Spanish
- Ability of the parent to give informed consent

Inclusion Criteria (continued)

- Permanent address, phone, email, alternate contact information, and primary care provider for next year
- Some exceptions to “permanent” info:
 - Parents who are college students
 - Military personnel NOT expecting to be deployed in next 12 months
 - Families who plan to move locally in next 12 months

Exclusion Criteria

- Parent does not agree to collection of nasal swab specimen or future use of the specimen
- Parent does not agree to sign medical records release authorization form
- Child has previous hospitalization for lower respiratory tract infection
- Known heart-lung disease, immunodeficiency, immunosuppression, or chronic GI disorder (except for reflux and constipation)
- Gestational age <32 weeks

Enrollment Goal

- **150** per site who meet all study enrollment requirements by **June 2017**:
 - Written informed consent
 - Medical records release authorization
 - Interview data
 - Nasal swab
- Convenience sample
- Agree to long-term follow-up

Spanish Speaking Participants

- All interview forms are being translated into Spanish
- Translated forms are meant to be read to participants in Spanish, but data are recorded in English into REDCap
- Participants will indicate their preferred language for follow-up on Contact Form

Data Entry: REDCap

- All data to be entered into *Research Electronic Data Capture* (REDCap)
- We strongly recommend that you enter data real-time

Identify Potential Participants

- Identify outpatient practice(s) and develop mechanism to introduce study to potentially eligible patients
- Develop system to monitor outpatient visits
- Call potentially eligible patients before their scheduled visit to determine interest

Scheduling Form

- Tool for sites to document and track:
 - Date/time of next clinical visit
 - Telephone and email correspondence
 - Date/time of study enrollment visit
 - Visit attendance and status (e.g., visit complete, visit incomplete)
- Data will be used by EMNet to monitor enrollment

Scheduling Form (continued)

Item	Can generate a report to...
<i>BEFORE SCREENING CALL</i>	
Date/time of next scheduled clinical appointment	monitor upcoming clinical visits and plan screening calls accordingly
Telephone and email correspondence	identify those for whom a contact attempt is due
<i>AFTER SCREENING CALL</i>	
Date/time of study enrollment visit	plan your visit a schedule and ensure you don't double-book
Visit attendance and status	know how many people have been enrolled and the status of the enrollment; alert EMNet to request participant payment

Screening Form

- Fill out for everyone screened via phone
- Brief introduction to study
- Confirms child's eligibility
- Screening Form ID # assigned by REDCap
- Insert child's name for questions with “[*child*]”

Screening Form (continued)

- Ask ALL questions even if you discover that child is ineligible (i.e., complete entire 10-question screening form)
- Last question (confirming enrollment) is left blank until after the *in-person* informed consent process

Screening Form (continued)

If child eligible & parent interested:

- Provide instructions to bring a diaper with stool to the visit. Offer to send written instructions.
- Arrange a time to meet ahead of their scheduled visit; record on Scheduling Form.
- Ask if parent has time to do the enrollment telephone interview.

Screening Form (continued)

If parent is NOT interested in participating:

- Record the main reason they do not want to participate
- Remind them of the date/time of their scheduled *clinical* visit
- Record on Scheduling Form that no visit is scheduled because parent is not interested

Enrollment Phone Interview

- Ideally done before the in-person visit, if parent has time (15-20 minutes)
- Interview about child health history, environment, and maternal pregnancy & nutrition information
- In order to minimize “unknown” as a participant response, please do not read “UKN” as an option to participant
- Consent implied through voluntary completion of the interview

Interview – Ethnicity / Race

- Self-identified
- If a participant says that he/she is of Latino/Hispanic origin and their race is "other" ask follow-up questions to help determine race (e.g., white Hispanic)

Breathing Problem

You may recognize breathing problems when [*child*] is coughing a lot, or breathing faster or breathing harder than normal. [*Child*]'s health care provider may even hear wheezing (high-pitched whistling sounds when breathing out) and have said that [*child*] has bronchiolitis, wheezy bronchitis, reactive airways, asthma, or pneumonia. When we say “breathing problems” we are talking about more than a stuffy nose. We are talking about episodes where the coughing wakes [*child*] at night (or may even cause vomiting), *or* when [*child*] has wheezing, *or* shortness of breath.

Enrollment Phone Interview (cont.)

- Maternal pregnancy & nutrition questions apply to biological mother
- Anyone with knowledge of biological mother health and nutrition (e.g., partner) may answer questions
- If non-biological mother responds to questions and does not know specific answer, utilize “unknown” response option

Interview – Age ≥ 6 months

- For children enrolled at age ≥ 6 months, a series of nutrition questions will pop-up in REDCap
- For younger children, these questions will be asked at the age 6 month follow-up interview (conducted via phone)
- Because age of enrolled children varies, and we need to put data into specific age groups, the questions refer to precise months of age (eg, 0-2.99 months)

Enrollment Phone Interview (cont.)

- Decline further participation in the study before completion of interview

If yes → briefly explain

- Interviewed, but later determined to be ineligible (eg, prior hospitalization for bronchiolitis)

If yes → briefly explain and clarify which Screening Form question(s) were answered incorrectly

Enrollment Visit

- Informed consent
- Medical Records Release Form
- Contact Form
- Enrollment Visit Form
- Specimen collection
- Tracking Form

Informed Consent

- Should be done before any study procedures are performed in-person
- Should be a thorough discussion of responsibilities
- Must consent to data sharing and future use of specimens
- Consent to genetic testing is optional

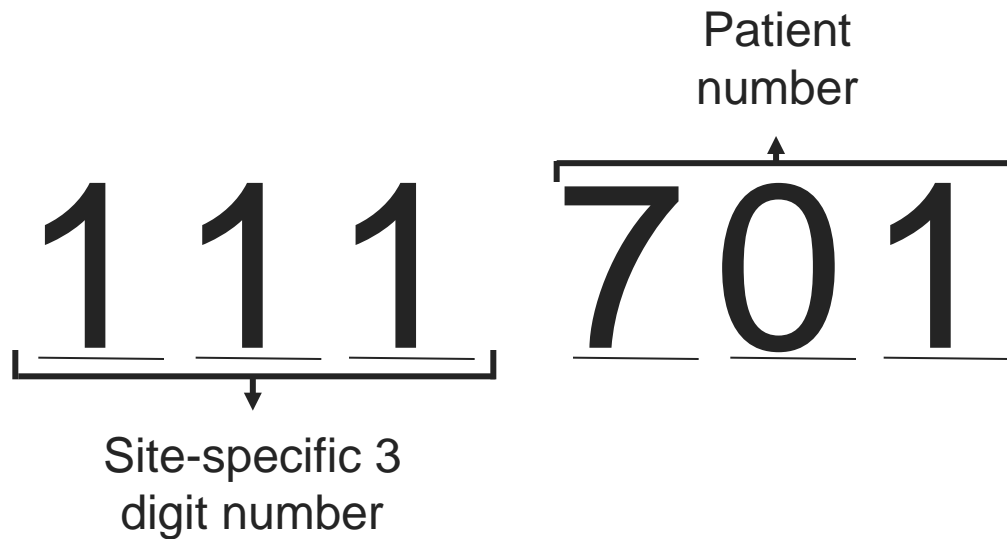
Medical Records Release Form

- Medical Records Release Authorization Form is required
- Release for “all providers” at “healthcare facilities” so that we can collect medical records from primary care clinicians and other specialists who may be outside your hospital
- Upload signed forms into REDCap (Tracking Form)

Study ID

- After Consent Form signed → answer the last question on Screening Form, which confirms enrollment
- Assign each enrolled participant a unique Study ID #
- Record the study ID # on Screening Form

Study ID # (continued)



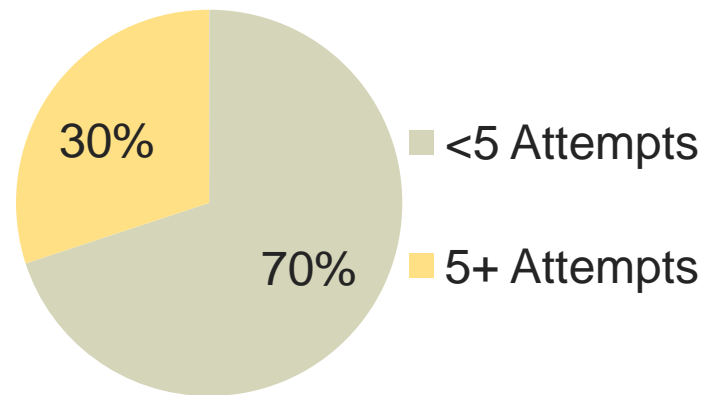
Contact Form

- Extremely important for long term follow-up to collect as much information as possible
- Required:
 - Phone, mailing address, email
 - PCP name and contact info
 - 1 alternate contact
- Note: email and alternate contact info can be given as late as the 1-week phone call

Follow-up Call Attempts

Reached in <5 attempts:

- 6-month follow-up call: 79%
- 12-month follow-up call: 70%
- 18-month follow-up call: 65%
- 24-month follow-up call: 69%
- 36-month follow-up call: 70%
- **Total follow-up calls: 70%**



Contact Form - Preferences

- Language: Spanish or English?
 - If patient is possibly someone who speaks predominantly Spanish, ask question
 - If question does not appear relevant, check “English” and don’t ask question
- Form of communication: phone and text
- Record preferred days of the week and times to call

Contact Form – SSN

- Required for payment
- Not required if parent willing to participate without remuneration
- Reassure parent that SSN will remain strictly confidential

Participant Remuneration

- Parent will receive payments via check for their time and travel expenses (e.g., parking costs)
- Families that live >25 miles from the site of the exam will receive an additional \$25 in appreciation of the additional travel time and costs incurred
- EMNet will process all remuneration check requests

Enrollment Visit Form

Form collects information about:

- Current symptoms and recent medication use (e.g., antibiotics) that are relevant to future specimen analysis
- Whether or not parent brought diaper to visit

Tracking Form

- Used to track participant status at enrollment and beyond. Mechanism to communicate:
 - Status changes (e.g., participant withdrawal)
 - Permanent opt out of sample collection
 - Known changes in custody
- Maintained by both site and EMNet

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Specimen Collection – Overview

Specimens collected at enrollment:

1. Nasal swab*
2. Saliva swab
3. Stool

* Required to be fully enrolled in study

Specimen Checklist

- Collects details about each specimen collected
- Prompts users if specimens are missing
- Must be completed after enrollment visit

Labels

- Make sure the Study ID # matches the # on the labels
- EMNet will send 10 labels to sites pre-printed with study ID
- Wrap a strip of clear tape over the label to prevent the label from falling off

Label use	Label amount
Consent forms	WRITE
Stool	4
Nasal swab	1
Saliva swab	1
Extra labels	4
TOTAL	10

Label all specimens!

Nasal Swab

- Collect the Nasal Swab specimen following instructions in protocol “Appendix E2. Swab Procedures”
- Collection procedures identical to MARC-35
- Nasal Swab Instructional Video:
<http://www.windstudy.org/whats-involved/swab-video/>

Saliva Swab

- If possible, wait to collect a saliva swab until 30 minutes after the child has eaten.
- Nursing or bottle-feeding within the last 30 minutes is acceptable.
- If the child ate a snack (e.g., crackers) within the last 30 minutes, please ask parent to give child a sip of water to ensure no food particles remain in the mouth.

Saliva Swab

- Peel open pouch from the side marked with the arrow
- Do not touch swab tip
- Place swab in the cheek pouch, rotate and move the swab head for 30 seconds. Collect from other points in the mouth where saliva pools

Saliva Swab

- Remove swab and insert swab into vial with preservation reagent
- Break off the swab shaft end at the molded break point and discard the shaft (non-swab end)
- Detailed instructions in protocol “Appendix E2. Swab Procedures”

Swab Storage & Shipment

- Nasal and saliva swab specimens will be stored on-site
- Place swabs in -80° C freezer within 24h of collection
- Frozen swabs should be shipped to MGH in batches with other specimens

Diaper Stool Collection - Parent

During screening phone call ask parent to:

- Collect 1 (or more) diaper(s) with stool within 24h before visit, close diaper(s), and place in a Ziploc (or similar) bag.
- Ideally we need:
 - $\frac{1}{4}$ teaspoon of stool
 - Diaper with stool and no urine (but we would rather have mixed diaper than no diaper)

Diaper Stool Collection - Parent

- Diaper must not have baby wipes or other objects (e.g., tissues) in it
- Write date and time the diaper was removed from the child on the outside of the bag (or on a piece of paper inside the bag)

Diaper Stool Collection - Parent

- Put bag with diaper in freezer
- Parent can double-bag diaper, if concerned
- Reassure them that this is for short-term storage



Diaper Stool Collection - Parent

- Please review the FAQs listed on the parent instructions.
- Remind parent to bring diaper with them to their visit!

Diaper Brought to Visit

Determine action based on diaper type

Diaper Description	Stool Quantity	Urine Present	Baby wipe or other object in diaper	Action
Optimal	$\geq \frac{1}{4}$ teaspoon	No	No	KEEP
Not Optimal	$< \frac{1}{4}$ teaspoon	Yes	No	KEEP
Ineligible	Any	Yes/No	Yes	DISCARD
Ineligible	Smear	Yes/No	No	DISCARD

Diaper Brought to Visit

Select the best diaper:

- If an “optimal” diaper is available, use that diaper and discard other diapers.
- If a single, “not optimal” diaper is available, use that diaper. If multiple, “not optimal” diapers are available, select the diaper with an adequate amount of stool and the least amount of urine.

Diaper Brought to Visit

If you have more than one diaper with $< \frac{1}{4}$ teaspoon of stool, you may combine the stool from these diapers in a single storage tube *if the diapers were all removed from the child within the past 24 hours.*

Stool Collection

- Thaw diaper to the point where you can collect stool (either with spoon attached to the lid of the collection container or tongue depressor)
- Do not touch inside of the collection container or the sterile spoon with your gloves
- Do not aggressively scrape diaper (we don't want diaper fibers mixed with sample)

Stool Collection

- Fill container with at least 6-7 spoonfuls
- Even with large sample, you don't need to fill container more than halfway
- If more stool is available, fill additional containers, up to 3 times (total of 4 sample tubes)

Forgotten Diapers

Options if parent forgets to bring a diaper with stool to the visit:

- Parent comes back with a diaper
- Site give a stool collection kit to parent; parent will mail the kit with specimen to EMNet
- Study staff pick up a diaper at specified location

Forgotten Diapers – Home Kit

If parent opts to use the home stool collection kit (for sample collection at home after the visit), give parent:



- Printed instructions
- OMNIgene Stool Specimen Form
- Collection kit with tube you pre-label

Forgotten Diapers – Home Kit

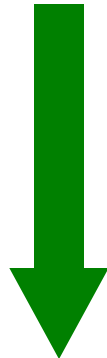
- Kits are pre-paid and pre-addressed; will be received and processed by EMNet
- Tubes do NOT have to be frozen at home after sample added; shelf-stable
- Kits are expensive, so please use as needed but do not distribute to all comers

Stool Storage & Shipment

- Place stool containers in -80°C freezer within 48h of diaper collection (or within 24h of receipt on-site), if not sooner
- Frozen stool should be shipped to MGH in batches with other specimens

Where to ship specimens if:

- Fully enrolled
- Found ineligible*
- Did not fulfill enrollment requirements*
- Withdrew after enrollment visit*



MGH

Withdrew enrollment
visit



**Do NOT ship –
destroy specimens!**

* Unless otherwise specified by your site-specific consent form

Deviations/Adverse Events

- There are protocol deviation and adverse event forms in REDCap for you to use
- Major protocol deviations need to be reported by email to Ashley Sullivan (EMNet) within 48 hours. EMNet will report to Dr Togias (NIAID).
- Serious AE need to be reported by email to Ashley Sullivan within 24 hours. EMNet will report to Dr Togias (NIAID).

afsullivan@partners.org

Enrollment Recap

1. Using site-specific practices, identify and contact parents of healthy infants to assess interest in study
2. Complete Screening Form, schedule enrollment visit, and do Pre-Visit Interview
3. At enrollment visit, review Informed Consent, complete Medical Records Release Authorization Form, assign study ID, complete Contact Form, Enrollment Visit Form, Specimen Checklist, and Tracking Form
4. Collect the specimens (swabs, stool)

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After Enrollment

- 1-week follow-up calls (as needed for PCP and alternate contact information)
- Follow-up with participants who forgot to bring diaper to enrollment visit
- Annual search of medical records in your healthcare system

Annual Records Request

- Each year, acquire available medical records in your hospital system:
 - ED notes
 - Inpatient discharge summaries
 - Outpatient visit notes (PCP, allergist/ immunologist, pulmonologist, ID specialist, or nutrition)
 - Laboratory results, microbiology, radiology, spirometry
- Send records to EMNet for review

Annual Records Request (continued)

- If records are NOT available in your system, **EMNet** will request records directly from these “outside” providers and institutions
- Each participant must have a completed medical records release form uploaded in REDCap
- EMNet will perform chart review

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- Can be used at bedside (no paper)
- Built-in branching logic to ensure proper sequence of questions
- Interviewer prompts helps flow of interviews

Screening Database

- Enrollment Scheduling Form
- Screening Form
- Pre-visit Interview

Participant Database

- Tracking Form
- Contact Form
- Enrollment Visit Form
- Specimen Checklist
- Protocol Deviation Report Forms
- Adverse Event Case Report Forms

Getting Started

- Send completed Electronic Data Capture Use Agreement to EMNet
<https://rc.partners.org/sites/default/files/content/docs/ERIS%20EDC%20User%20Agreement.pdf>
- Access granted by Partners (MGH)
- Firefox or Chrome strongly recommended as browser
- Log in at <https://redcap.partners.org>

Getting Started (continued)



Log In



FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL
AND MASSACHUSETTS GENERAL HOSPITAL

Partners HealthCare Users: Login with your Partners username and password.

If you require your Partners password reset: [Password Self Service](#)

All other users can reset their passwords by clicking on the "Forgot your password?" link below.

Partners HealthCare and REDCap usernames and passwords are unique to YOU. They must not be shared with anyone.

Please log in with your user name and password. If you are having trouble logging in, please contact [Partners HealthCare EDC Support](#).

Username:

Password:

Log In

[Forgot your password?](#)

Saving Records

- **Incomplete** → no data entered
- **Unverified** → data entry partially complete
- **Complete** → data entry complete

Saving Records (continued)

- Save frequently!
- After saving a form, a pop-up box will appear if a response is missing in a required field
- Return to that field and enter a response

REDCap Questions?

- Problems logging in?

Contact Partners HealthCare EDC Support

edcsupport@partners.org

- New user requests, other issues, or questions?

Contact Catalina Gimenez-Zapiola

cgimenez-zapiola@partners.org

617-643-7652

Training Log

- Training logs will be sent so that site PIs can attest to study staff training
- Training Elements:
 - General Training
 - REDCap practice database use
 - Nasal Swab Collection Video
 - Manual of Procedures

Questions?

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