

Aerosols from harmful algal blooms: Exposures and health effects in highly exposed populations

OMB Control No. 0920-1316

Non-substantive change

Supporting Statement Part B –

Collections of Information Employing Statistical Methods

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Part B. Collections of Information Employing Statistical Methods

B.1. Respondent Universe and Sampling Methods

Respondents include adults at least 18 years of age, who are exposed to aerosols generated during harmful algal blooms (HABs) while living near or working in Florida.. We will not exclude pregnant women who volunteer to be part of the study. We will not recruit children because we are interested in occupational and community exposures. We will not recruit prisoners as respondents must be able to move freely outdoors. We will recruit 200 respondents.

CDC will recruit a convenience sample. Sampling methods were discussed with Drs. David Olson and Dana Flanders, statisticians with NCEH. There is very little information about human exposures to and health effects of aerosols generated during HABs. Thus, we concluded that it is not necessary to use extensive resources to identify all the potential, eligible study participants and chose a random subset to enroll in the study. Rather, any information we collect using convenience sampling will advance the science of HABs and public health and will lead to new hypotheses about HABs and health that can be explored in future research.

Study power

Sample size calculations

There is considerable information in the literature about the health effects from exposure to marine HAB toxins. However, there is little information about the health effects from exposure to cyanobacterial toxins. Thus, we used a conservative estimate of the potential sample size needed for this study, by using data from Falconer et al (1983). Falconer et al (1983) compared clinical test results for liver enzyme levels in hospitalized patients in an area served by a drinking water source with an ongoing *Microcystis aeruginosa* bloom with test results from hospitalized patients from an area with no bloom in the drinking water source. *M. aeruginosa* produces microcystins, which are potent liver toxins that induce changes in blood levels of liver enzyme.

Approximate concentrations of liver enzymes in study by Falconer et al. (1983). Bolded numbers show increases during bloom compared with before the bloom in populations exposed or unexposed to drinking water from a source with a *Microcystis aeruginosa* bloom.

Enzyme (μ /L in plasma)	Residents with Malpas Dam water supply (exposed). Values estimated from graph. N=145	Country residents with different water supply (unexposed). Values estimated from graph. N=145
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	Before Bloom, mean (SEM)	During Bloom mean (SEM),	Before Bloom, mean (SEM)	During Bloom, mean (SEM)
GGT	43 (4)	102 (18)	60 (8)	55 (8)
ALT	25 (4)	36 (8)	30 (3)	30 (4)
AST	24 (3)	26 (3)	26 (3)	24 (2)
AP	71 (2)	72 (3)	81 (2)	87 (3)

SEM = standard error of the mean

Assumptions for calculation assuming simple random sample:

- Random sample
- Independence of data
- Sample size of 871 evenly distributed across three time-periods and 2 places (6 total)
 - o N=145 (12)
- NOTE: Repeated measurements formula would need to include the estimated variance of the differences

Formulas:

Two-tailed test:

$$n = \left[\frac{(Z_{\alpha/2} + Z_{\beta})\sigma}{E} \right]^2$$

$Z_{\alpha/2} = 1.96$ for 95% confidence

$Z_{\beta} = 0.84$ for 80% power

power = $(1-\beta) \times 100$

σ = estimated variance

$\sigma = \sqrt{n} \times \text{SEM}$

E = maximum error of estimated mean (or null) vs alternate hypothesis values (from paper)

One-tailed test:

$$n = \left[\frac{(Z_{\alpha/2} + Z_{\beta})\sigma}{E} \right]^2$$

$Z_{\alpha/2} = 1.65$ for 95% confidence, one-tailed test

$Z_{\beta} = 0.84$ for 80% power

power = $(1-\beta) \times 100$

σ = estimated variance

$\sigma = \sqrt{n} \times \text{SEM}$

E = maximum error of estimated mean (or null) vs alternate hypothesis values (from paper)

Estimation of sample size using results from study participants before and during exposure

Enzyme (μ /L in plasma)	$Z_{\alpha/2}$	Z_{β}	σ	E	N: two-tailed test	N: One-tailed test
GGT	1.96	0.84	48	59	5	4
ALT	1.96	0.84	48	11	149	117
AST	1.96	0.84	36	2	2,520	2007
AP	1.96	0.84	24	1	4,515	3571

Formula:

Summary of sample size considerations:

Our planned sample size of 150 participants should give more than 80% power to detect changes (i.e., approximately a doubling) in liver enzyme levels with 95% confidence, assuming that the values will increase with exposure.

B.2. Procedures for the Collection of Information

We will recruit a convenience sample of 200 study participants from the subpopulation comprising adults at least 18 year of age, who are exposed to aerosols generated during HABS while living near or working in Florida.

Study participant inclusion criteria are as follows: the individual must be at least 18 years old, understand English, Spanish, or Haitian Creole, spend at least 2 hours a day outside each day, be able to do a lung function test, and be willing to do all study activities listed in the screening survey. Study participant exclusion criteria are as follows: the individual is less than 18 years old, cannot understand English, Spanish, or Haitian Creole, does not spend at least 2 hours a day outside each day, is unable to do a lung function test, and is unwilling to do all study activities listed in the screening survey.

Study staff, including NCEH staff and contractors will interact with study participants to collect screening survey, survey data, and other data. Details about who will collect the information and how the collection will occur (how it is done) is in Table B.2.1. below.

Table B.2.1. Summary of information & materials to be collected and who will collect them. There will be 5 study days, one at the beginning of the bloom, 3 during the bloom, and one near the end of the bloom. For study days 1, 3, and 5, we will collect blood in addition to the survey responses, biospecimens, and environmental samples.

Information & materials to be collected	Collected by	Number of times information and materials collected per participant N = 200 respondents	Data to be collected
Telephone Screening/Baseline Survey	Study staff (CDC staff and contractors)	1	Whether or not an interested person meets study inclusion criteria and baseline data
Symptoms Survey	Study staff	10	Health symptoms, other relevant exposures, etc.
Dock air samples	Study staff	5 (one for each of 5 study days)	Gases and vapors emitted as blooms die off and HAB toxin levels
Personal air samples	Study staff	5 (one for each study day)	HAB toxin levels
Water samples	Study staff	5 (one for each study day)	Algal taxonomy and HAB toxin levels
Nasal swabs	Study staff	10	HAB toxin levels
Lung function test	Study staff	10	Lung function parameters
Blood samples	Registered phlebotomist	3	Liver enzyme levels, creatinine levels
Urine samples	Study participants	10	HAB toxin levels
Fish	Study staff (who will forward to EPA)	≤5 (one for each study day when respondent is fishing)	HAB toxin levels in fish

Record of time spent outdoors	Study participants	5	Hours spent outdoors
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Interviewers will be trained by CDC staff to oversee and/or conduct, as appropriate, study activities.

Respondents will be recruited using a flyer (Attachment 4 - Flyer) placed in areas where Florida Department of Protection staff will see them, where fishing charters are arranged, and where fishing boat crews congregate. A Screening/ Baseline Survey (Attachment 5 - Screening/Baseline Survey) will be used to screen potential respondents for interest and eligibility. Consent to participate in the investigation will be obtained using a paper consent form (Attachment 6 - Consent Form), which the respondent will read and sign. The consent forms will provide the following information: purpose of the data collection, list of activities for respondents, description of risks, data/information disclosure possibilities, description of benefits, compensation, treatment for injury, contacts for questions, and a statement about voluntary participation, refusal, and withdrawal.

If someone meets our inclusion criteria and agrees to participate, we will ask them to do the following:

- Read and sign a consent form (Attachment 6 - Consent Form)
- Make 5 appointments with study staff to do study activities (study days 1, 2, 3, 4, and 5; NOTE: days not consecutive but occur across bloom season—one day at the beginning of the bloom, 3 during the bloom, and one at the end of the bloom)
- On study days 1, 3, and 5:
 - o Provide a blood specimen for liver enzyme levels and creatinine levels in the morning (Attachment 8 -Providing Blood Specimen)
 - o Receive training on how to collect a urine sample (one time only)
 - o Do the following in the morning and evening:
 - Complete symptom survey (Attachment 7 - Symptom Survey)
 - Provide urine specimen for HAB toxin levels (Attachment 9 - Providing Urine, Lung Function Test, Nasal Swabs)
 - Perform lung function test
 - Provide nasal swab for HAB toxin levels
 - o Wear a personal air sampler during the day (Attachment 10 - Be Outfitted with Personal Air Sampler)
 - o Record time spent outdoors using our form (Attachment 11 - Record of Time Spent Outdoors)
 - o Allow study staff to put air samplers (one for aerosols, one for gases and vapors (e.g., hydrogen sulfide) near their home or worksite (if respondent works on the water)
 - o At the end of the day, allow study staff to collect air monitoring equipment
 - o Provide a fish if they fish on the study day (Attachment 12 - Record of Fish for Analysis by EPA)
- On study days 2 and 4:

- o Do all study activities they do on study days 1, 3, and 5, except that they will not need to give us a blood sample.

We are requesting multiple responses from each participant for a number of reasons. We cannot predict when the HAB will bloom nor when or whether the bloom will produce toxins; thus, we will collect data over the bloom season. The blooms typically comprise different organisms over time, and we would like to assess exposure to the blooms as they evolve. Finally, we would like to know if the toxins or effects of the toxin accumulate or worsen over time as a person is exposed.

B.3. Methods to Maximize Response Rates and Deal with No Response

CDC staff recently attended a public meeting in Stewart, Florida and a federal and state agency meeting in Fort Myers, Florida where we learned of extensive public concern about HABs and health. Given the amount of media attention given to the blooms, and the community concern discussed at a meeting of local elected officials on May 7, 2019 in Stewart, Florida, we expect to be able to recruit 200 eligible study participants.

We plan to screen 250 potential participants for eligibility, 50 will not be eligible or will choose not to participate. Again, given the level of public concern, we expect to be able to recruit 200 eligible study participants. We will enroll people during an individual interview that will completely describe study activities (see Attachment 5 – Consent Form) to ensure that study participants know what is expected of them before they agree to participate.

B.4. Test of Procedures or Methods to be Undertaken

We pilot tested both the flyer and the survey with 9 individuals, including CDC staff (scientists and non-scientists). We did not make any changes to the forms as none were suggested. We used that pilot testing to estimate the time burdens acknowledged on the forms.

B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Individuals consulted on statistical aspects and individuals collecting and/or analyzing the data from this study are in Table B.5.1.

Table B.5.1. Individuals consulted on statistical aspects and individuals collecting and/or analyzing the data from this study

Name	Title	Affiliation	Phone	Email
Consultations outside the agency				
Lesley D'Anglada, DrPH, MEH	Senior microbiologist	Office of Science and Technology, U.S. EPA	202-566-1125	danglada.lesley@epa.gov
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Greg Boyer, PhD	Professor	SUNY College of Environmental Science and Forestry	315-470-6825	glboyer@esf.edu
Barry Rosen, PhD	Biologist	USGS, Florida	407-738-0669	brosen@usgs.gov
Andrew Reich	Marine Toxin Specialist	Florida Department of Health	813-307-8015 x 5961	Andy.reich@flhealth.gov
Alice M. Shumate, PhD, MPH LCDR	Co-Director, Center for Maritime Safety and Health Studies	Respiratory Health Division at NIOSH	Phone: 509-354-8018	wii5@cdc.gov
Kathleen Clark PhD MS RRT CPFT	Research Epidemiologist	CDC/NIOSH/RHD/ Surveillance Branch	(304) 285-5764	lln9@cdc.gov
Consultations inside the agency				
Stephanie Kieszak, MA, MPH	Statistician	National Center for Environmental Health (NCEH)	770-488-3407	skieszak@cdc.gov
Dana Flanders	Statistician	Emory University/NCEH	404-727-8716	flanders@sph.emory.edu
David Olson	Statistician	NCEH	770-488-3724	dolson@cdc.gov
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Individuals involved in collecting and/or analyzing data				
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