# Aerosols from cyanobacterial blooms: Exposures and health effects in highly exposed populations

OMB Control No. 0920-xxxx

New

Supporting Statement Part A –

Justification

Lorraine Backer
Senior Epidemiologist
Division of Environmental Health Science and Practice
Centers for Disease Control and Prevention
Phone: 770-488-3426
Email: lfb9@cdc.gov
Fax: 770-488-3410

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**Goals of the study:** Human exposures to cyanobacterial toxins have been reported to produce a variety of health effects, including respiratory irritation and liver and kidney damage. The goal of this study is to conduct exploratory analyses of the relationships between biomonitoring data, environmental data, and symptom reporting. We expect this research to be hypothesis generating and not necessarily generalizable to participants with similar exposures in the same population or to the public more generally.

**Intended use of the resulting data:** The data will add to the scant existing scientific literature on the human health impacts of exposure to cyanobacterial toxins.

**Methods to be used to collect data:** The methods used to collect data include telephone screening/baseline surveys to determine eligibility/collect baseline data. Respondents will complete symptom surveys with study staff, who will enter responses directly into the Center for Disease Control and Prevention's (CDC's) REDCap system. Using standard protocols, study staff will collect lung function test data and upload the resulting data into REDCap. Using standard protocols, study respondents will provide nasal swabs to analyze for cyanobacterial toxins and urine specimens to analyze for cyanobacterial toxins and creatinine. A certified phlebotomist will collect blood samples to analyze for liver enzyme (for liver damage) and creatinine levels (for

# A.1. Circumstances Making the Collection of Information Necessary

This is a new information collection request (ICR) from the National Center for Environmental Health (NCEH), Centers for Disease Control and Prevention (CDC). This data collection is authorized by the Public Health Service Act §301 (241) (Attachment 1). NCEH requests 3 years of approval.

**Background**

Algal toxins from cyanobacterial harmful algal blooms (HABs) include some of the most potent natural chemicals. People and animals are at risk for exposure to toxins produced by cyanobacterial harmful algal blooms (CyanoHABs) in drinking water (Falconer et al., 1983; El Saadi et al., 1995) or in improperly treated water used for medical purposes such as renal dialysis (Jochimsen et al., 1998; Carmichael et al., 2001). Additional potential exposure sources include contaminated dietary supplements (Gilroy et al., 2000) or fish harvested from lakes with ongoing CyanoHABs (De Magalhaes et al., 2001; Xie et al., 2005; Cazenave et al., 2005; Kann, 2008).

Although outbreaks of human illness associated with CyanoHABs were sporadically recorded for decades, information about clinical signs and symptoms from cyanobacterial toxin poisonings is primarily from animal poisonings and laboratory studies (Carmichael and Falconer, 1993). Exposures to cyanobacterial toxins produce a variety of symptoms and illnesses (Hunter, 1998; Falconer, 1998). The primary effects include acute hepatotoxicity, acute neurotoxicity, gastrointestinal symptoms, and respiratory, dermatologic, and allergic reactions. Which, if any cyanobacterial toxins cause respiratory symptoms is not known; however, cyanobacterial hepatotoxins or lipopolysaccharide endotoxins may be associated with the gastrointestinal disturbances (Sykora and Keleti, 1981).

A significant source of cyanobacterial toxin exposure is recreational use of contaminated fresh water bodies because large populations are likely to be exposed and toxins may occur in high concentrations. Initial epidemiologic studies did not find an association between recreational cyanobacteria exposure and adverse health effects (Phillip, 1992; Phillip and Bates, 1992; Phillip et al., 1992). However, Pilotto et al. (1997) reported that persons exposed for more than 1 h to recreational waters containing elevated concentrations of cyanobacteria (>5000 cells/mL) were more likely to report at least one symptom during the 7 days after exposure than were persons exposed to waters that did not contain cyanobacteria. More recently, Stewart et al. (2006b) found that persons who used personal watercraft on lakes with high cyanobacteria concentrations (cell surface area> 12.0 mm2/mL) were 2.1 (CI, 1.1–4.0) times more likely to

report symptoms, particularly respiratory symptoms, than were persons who used their personal watercraft on lakes with low cyanobacteria concentrations (cell surface area < 2.4 mm2/mL).

In the United States, the U.S. Environmental Protection Agency (EPA) provided guidance on acceptable levels of cyanobacterial toxins in drinking or recreational waters (EPA, 2019a, b). The World Health Organization (WHO), Australia, and some European countries have developed guidelines for managing recreational waters with cyanobacterial blooms (WHO, 2003; Chorus, 2005). However, these guidelines were based on cell concentrations rather than on cyanobacteria toxin concentrations, and not all cyanobacterial blooms produce toxins. Further, these are guidance levels, not regulatory levels. Data from epidemiologic studies designed to evaluate the associations among environmental cyanobacteria toxin concentrations, human biomarkers of cyanobacteria toxin exposure, and health symptoms are needed to develop more specific recreational exposure guidelines.

In a previous study of recreational microcystin (MC) exposure at a small lake CDC conducted in 2006, we recruited 104 study respondents from lake visitors planning recreational activities, such as boating and using personal watercraft, that would generate aerosols (Backer et al., 2008). During data collection for that study, MC concentrations within the bloom lake water were very low (<2–5 mg/L). Study respondents' plasma MC concentrations were all below the limit of detection (0.147 mg/L) for the enzyme-linked immunosorbent assay (ELISA) (Backer et al., 2008).

In 2007 CDC/NCEH conducted a study of recreational exposure to the toxins called microcystins among 81 children and adults planning recreational activities on either of three California reservoirs—two with significant, ongoing blooms of toxin-producing cyanobacteria, including *Microcystis aeruginosa* (Bloom Lakes), and one without a toxin-producing algal bloom (Control Lake) (Backer et al., 2010). We analyzed water samples for algal taxonomy, microcystin (MC) concentrations, and the presence of respiratory viruses (adenoviruses and enteroviruses). We measured MCs in personal air samples, nasal swabs, and blood samples. We interviewed study respondents for demographic and health symptoms information. We found highly variable MC concentrations in Bloom Lakes (<10mg/L to >500mg/L); MC was not detected in the Control Lake. We did not detect adenoviruses or enteroviruses in any of the lakes. Low MC concentrations were found in personal air samples (<0.1ng/m3 [limit of detection]–2.89ng/m3) and nasal swabs (<0.1 ng [limit of detection]–5ng). MC concentrations in the water-soluble fraction of all plasma samples were below the limit of detection (1.0mg/L). Our findings indicated that recreational activities in water bodies that experience toxin-producing cyanobacterial blooms generate aerosolized cyanotoxins, making inhalation a potential route of exposure (Backer et al., 2010).

Based on the results from our studies, we determined that future studies should include collecting nasal swabs to assess upper respiratory tract deposition of toxin-containing aerosols droplets. We also hypothesized that inhaled cyanotoxins, such as MC, may subsequently be

absorbed into the body through either upper or lower airway mucosal surfaces. However, we did not demonstrate a detectable internal MC dose as measured by plasma toxin analysis or a significant increase in self-reported acute symptoms after exposure. It is likely that healthy people will not have adverse acute effects from periodic exposures to MC in aerosols generated by water based recreational activities in lakes with patches of toxin producing blooms. However, these people may be exposed to potent hepatotoxins. We also hypothesize that other potent CyanoHAB toxins, such as anatoxin a or cylindrospermopsin may be incorporated into aerosols, inhaled and deposited in the body, presenting other, potentially synergistic, health risks. In addition, it is possible that swimming and other water-based activities that result in swallowing water present a higher risk for adverse health effects from ingesting cyanobacterial cells and extracellular toxins in the water.

In addition to cyanobacterial toxins, other chemicals produced by cyanobacteria, such as geosmin and methylisoborneal (MIB), may be present in aerosols generated during a CyanoHAB. Geosmin and MIB produce a musty odor and taste in water that is noticeable at very low concentrations. CyanoHABs may present additional health risks as they die off. Previous work done in Wisconsin demonstrated low but measurable concentrations of hydrogen sulfide and methane in the air near dense and decomposing cyanobacterial blooms (Dr. Mark Warner, personal communication, 2009). An earlier study of the effects of low levels of airborne hydrogen sulfide found that community members living in areas with persistent low levels of airborne hydrogen sulfide from local industrial activities reported more bronchitis, persistent cough, shortness of breath, and wheezing than people living in areas without this exposure did (Legator and Morris 2001).

The National Center for Environmental Health (NCEH), Centers for Disease Control and Prevention, requests a three-year Paperwork Reduction Act (PRA) clearance for a new information collection request titled “Aerosols from cyanobacterial blooms: exposures and health effects.” NCEH is generally authorized to conduct research under the Public Health Service Act, Section 301, “Research and investigation,” (42 U.S.C. 241) (Attachment 1).

We will conduct a cohort study of 200 people highly exposed to CyanoHABs in Florida. We define “highly exposed” as those exposed because of their occupation (e.g., lock gate keepers, fishing guides) and those exposed because they live on a canal or river and spend at least two hours outside on most days.

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/baseline 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/baseline survey.

Bloom composition and concentrations of toxins can vary over time during a bloom (Paerl and Otten, 2013) and CDC is interested in not only exposure, but also how exposure varies as the blooms develop, mature, and die off. Also, we cannot predict where a bloom may occur in a given timeframe. Thus, we will work closely with the Florida Department of Environmental Protection to identify when a bloom develops (either via limited routine monitoring or by visual indications followed by water testing for cyanobacteria and toxins). Once a bloom is verified, we will initiate the study (i.e., recruit and enroll respondents in collaboration with the Florida Department of Health) in the area affected by the bloom. Study staff will collect data from respondents in the morning and evening on 5 study days (day 1 during the beginning of a bloom, days 2-4 in the middle of the bloom, and day 5 toward the end of the bloom) between March and November.

The 60-day Federal Register Notice was published on September 17, 2019; and is further discussed in Section A8 (Attachment 2).

# A.2. Purpose and Use of the Information Collection

Environmental public health stakeholders, including public health officials, the medical community, local elected officials, and the public pose many questions about the associations between exposure to cyanoHABs and the associated toxins and health outcomes. There is scant available literature aside from the papers by Backer et al. (2008, 2010) that specifically try to explore these associations.

The purpose of this information collection is to conduct research on exposures and health effects from aerosols generated during cyanobacterial blooms. Human exposures to cyanobacterial toxins have been reported to produce a variety of health effects, including respiratory irritation and liver and kidney damage. The results from this research will enhance the body of knowledge about how exposure to cyanobacterial blooms may affect public health.

We expect this research to be hypothesis generating and not necessarily generalizable to participants with similar exposures in the same population or to the public more generally. The results from the proposed data collection help address some of the scientific questions associated with cyanoHABs, including the following:

- Can cyanotoxins be found in urine and on nasal swabs in people exposed to cyanoHABs?
- Can we identify markers of kidney and liver damage in people exposed to cyanoHABs?
- Can we explore reporting of acute symptoms and determine whether we can generate hypotheses about the relationship between those symptoms and exposure, including related to changes over the bloom season.
- Are environmental levels of cyanotoxins predictive of what we can find in people?

Sample size calculation of N=200 was based on the one available study on changes in liver enzyme values following exposure to microcystins in drinking water (see Supporting Statement B). For the other endpoints, (e.g., respiratory, gastrointestinal symptoms) we will report descriptive statistics because data are not available for power calculations.

If NCEH does not collect the information described for this study, gaps in knowledge about using biomonitoring to exposure exposures to aerosols contaminated with cyanobacterial toxins and the potential health effects will remain.
The information collected will be broadly applicable to other geographic regions experiencing cyanobacterial blooms in waters widely used by the public. The organisms comprising CyanoHABs tend to be from a widely known group of cyanobacteria and, while the organisms comprising a specific bloom will vary, they are likely to contain organisms similar to the ones we will identify in this study.

**Purpose of collecting samples and specimens**

Environmental samples, particularly the air samples, will be used to verify human exposures to aerosols contaminated with cyanobacterial toxins that are generated during CyanoHABs. The toxins have no odor or taste, thus environmental sample collection and analysis is needed to demonstrate exposure.

We will collect fish from respondents who fish during their study day(s). This will allow quantitative analysis of the fish for cyanobacterial toxins. This information will be valuable in assessing potential human exposures from seafood.

Human biomonitoring using nasal swabs, lung function tests, urine, and blood is needed to assess the amount of cyanobacterial toxins are in the bodies of people who are exposed to the aerosols generated during CyanoHABs. The biomonitoring results will help us understand what doses of the cyanotoxins are relevant to human health endpoints such as respiratory irritation or liver damage. The results from biomonitoring data collected in the morning are expected to be different from those collected during the evening after respondents have been outside and exposed to aerosols from the CyanoHABs. By collecting biomonitoring data during different stages of a CyanoHAB, we will be able to assess trends in the values of biomonitoring data across the bloom season.

**How data will be analyzed**

Results from symptom surveys, blood and urine specimens, nasal swabs, lung function test results, and water, air, and fish samples will be analyzed using univariate methods to

summarize the data. CDC staff will compare the following information to determine if there are changes or correlations: 1) individual's morning results with evening results, and 2) biomonitoring results with cyanotoxin levels in air, water, and fish. CDC staff will assess environmental and biomonitoring over time.

For short-term effects (e.g., self-reported symptoms), study respondents can serve as their own controls. For the cumulative effect on pulmonary function tests, we will use a comparison group from NHANES for the most appropriate demographics, season, and geographic area (e.g., southeastern U.S. or Florida).

For long-term effects (e.g., changes in liver enzyme concentrations), study respondents will experience cumulative exposures over the study period. There is some evidence of seasonal variation in liver enzyme concentrations from a study in Japan (Miyake et al., 2009). The authors used approximately 1,270,000 test results collected over seven years from one hospital and reproduced with an additional 215,000 test results collected over 2 years from another hospital. The serum levels of liver enzymes tended to increase in the winter. For example, serum levels of AST and ALT increased about 6% in men and about 5% in women in tests done in winter when compared with results from tests done in summer. For our study, respondents will serve as their controls (i.e., beginning of bloom compared with late in the bloom). We will use NHANES liver enzyme data stratified by the season of sample collection and clinical values for creatinine as additional comparison values.

# A.3. Use of Improved Information Technology and Burden Reduction

To reduce the burden on study respondents, CDC will use electronic data entry for 77% (188 of 244 burden hours) of the burden hours. Specifically, the screening/baseline/baseline survey (Excel), and CDC staff will collect survey responses directly into the CDC's instance of the survey platform REDCap. Data entry for the remaining 23% of the burden will be paper and pencil collection. To enhance the ease of data recording, the survey will include automatic skip patterns. Study staff will simultaneously collect survey data on a paper form which will be compared with the data in REDCap to ensure accuracy and then destroyed. CDC will also embed appropriate ranges for questions with numerical answers to limit data entry or transcription errors.

Additional considerations for field work conducted while the COVID-19 pandemic is still active.

This protocol has been updated to reflect changes necessary to start the Cyano Aerosol study during the COVID-19 pandemic. Appropriate safety precautions, including the use of all appropriate additional personal protective equipment (PPE), will be implemented to keep the study team and participants safe during the study data and sample collection. Additional procedures will be implemented during recruitment and field work to ensure that the Cyano

Aerosol Study continues in compliance with CDC, state, and local requirements are noted in https://www.cdc.gov/coronavirus/2019-ncov/hcp/non-covid-19-client-interaction.html for non-COVID-19

The activities that will be modified include:

- Ensuring that social distancing and the use of PPE are employed to comply with CDC and state guidelines during face-to-face recruitment activities, if they occur.
- Adding additional information to the recruitment letter and consent documents to reassure potential Cyano Aerosol Study participants that all state and CDC guidelines will be followed.
- Asking participants about their and their family members' COVID-19-status during their appointment reminder phone call and prior to collecting any study-related data.
- Monitoring the temperature of Cyano Aerosol Study team members (CDC/NCEH and contractor staff) twice daily on study days and taking participant's temperatures prior to any in-person interactions with study participants (spirometry training on study day 1 for each participant).
- Administering the questionnaire over the phone instead of in person to reduce exposure time.
- Administering spirometry testing remotely rather than in person to reduce exposure time.
- Asking study participants to the diary of time spent outside and urine specimens outside for contact-less pickup by study staff.

These changes are provided in the following modified Cyano Study Attachments: Flyer (Attachment 4), Screening/Baseline Survey (Attachment 5), and Consent form (Attachment 7). We have added additional questions about body temperature and whether the study participant or any household members have COVID-19-related symptoms or are currently sick with COVID-19.

CDC added the following (based on OMB-approved language from Frank Bove's PFAS study and modified for this study) to the study flyer, the screening/baseline survey, and consent form:

Please be assured that CDC will take COVID-19 prevention measures at every step of our work in your community. The study will be conducted following all state, local, and CDC guidelines in place at the time the study is conducted. CDC team members will be monitored twice daily for fever and any COVID-19-related symptoms. Any team members with fever or COVID-19-related symptoms will not be allowed to collect data until they have quarantined for the recommended period, if appropriate, and have tested negative for COVID-19. There will be times when study staff will visit your home to collect information (study forms, urine specimens, personal air samples). If there is any face-to-face contact with study staff at that time, study team members will wear surgical masks and gloves and study participants will wear

a face covering or mask. If you do not have a mask, one will be provided to you. If you are unable to wear a mask for medical reasons, you can let us know.

## A.4. Efforts to Identify Duplication and Use of Similar Information

CDC consulted with our federal partners at the U.S. Geological Survey and the U.S. Environmental Protection Agency and the information collections proposed for this study are not being done elsewhere. CDC is not aware of any other studies utilizing this protocol.

CDC conducted literature and World Wide Web searches and did not identify studies collecting the information proposed here.

## A.5. Impact on Small Businesses or Other Small Entities

This data collection will not involve small businesses.

## A.6. Consequences of Collecting the Information Less Frequently

The respondents will do the study activities for this information collection on 5 study days (some responses will occur twice in each study day). The first study day will be during the period just after the bloom is identified and the other 4 will occur during mid-bloom and after the bloom has ended. The study days will occur over a period of months (e.g., March through November) and will hereafter be noted as study days 1, 2, 3, 4, and 5.

CDC is requesting multiple responses for a number of reasons. We cannot predict when the CyanoHAB will form, nor can we predict when a CyanoHAB might 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. The consequences of collecting the data less frequently include that we would not be able to assess exposures as they change over time nor will we be able to look at how health effects change during the duration and evolution of the bloom.

There are no technical or legal obstacles to reducing burden.

# A.7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The following special circumstance(s) apply to this information collection. We are requiring the following: Respondents will report information to the agency more often than quarterly.

CDC is requesting multiple responses for a number of reasons. We cannot predict exactly how a cyanobacteria bloom will develop or die off. Thus, we will collect data over the bloom season. The blooms typically comprise different organisms and produce different toxins 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.

# A.8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

A. A 60-day Federal Register Notice was published in the *Federal Register* on September 17, 2019, vol. 84, No. 180, pp. 48929-48931 (Attachment 2). CDC/ATSDR received a total of 162 public comments, including 3 substantive comments. The comments and the CDC/ATSDR response is provided. Based on the comments received, CDC made a number of changes to the protocol (Attachment 2a).

B. The following people outside and inside the agency were consulted to obtain their views on the availability of data, frequency of collection, the clarity of instructions, and on the data elements to be reported.

**Table A.8.1 External and internal consultations for this data collection.**

| 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 |
| Keith Loftin, PhD | Water quality specialist | U.S. Geological Survey (USGS), Kansas Water Science Center | 785-832-3543 | kloftin@usgs.gov |
| 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 | 813-307-8015 x 5961 | Andy.reich@flhealth.gov |

| | | | | |
|---|---|---|---|---|
| | | Health | | |
| Alice M. Shumate, PhD, MPH<br>LCDR | Co-Director, Center for Maritime Safety and Health Studies | Respiratory Health Division at NIOSH | Phone: 509-354-8018 | wii5@cdc.gov |
| Kathleen Clark<br>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 |
| Elizabeth Hamlin | Research Chemist | Division of Laboratory Sciences, NCEH | 770-488-7082 | ehamlin@cdc.gov |
| Kanta Sircar | Epidemiologist | NCEH | 770-488-3384 | ksircar@cdc.gov |

# A.9. Explanation of Any Payment or Gift to Respondents

Below is an explanation of study activities that were used to justify the incentives for respondents.

Based on study activities and previously approved OMB data collections, we will provide study participant incentives as shown in Table 3 below. The incentives will be in the form of gift cards given to respondents as they complete the study activities.

To guide decisions about incentives, we used previous OMB-approved incentives listed here.
**Table A.9.1. Study participant incentives.**

| Study Activity | Number of times study participant does the activity | Incentive for each time study participant does the activity | Total incentive for activity |
|---|---|---|---|
| Complete survey | 10 (twice on all study days) | $10 each study day after completing both surveys | $50 |
| Provide blood specimen for liver enzyme levels and creatinine | 3 (on study days 1, 3, and 5) | $75 after the third blood draw | $75 |
| Complete record of time spent outdoors | 5 | $5 | $25 |
| Provide urine and nasal swab for cyanobacterial toxins, do lung function test | 10 (twice on all study days) | $30 on each study day after providing both urine specimens | $150 |
| Provide fish | 1 time during study | 0 | 0 |
| TOTAL | | | $300 |

If all parts of the study are completed, respondents will receive a total of $300 in gift cards. Respondents will be asked to sign a receipt in a standard receipt book to indicate that they acknowledge receiving the gift card each time the receive one.

# A.10. Protection of the Privacy and Confidentiality of Information Provided by Respondents

## A.10.1. Privacy Impact Assessment

This project was reviewed by the NCEH Information Security Systems Office for applicability of the Privacy Act by the CDC Chief Privacy Officer. The Privacy Act does apply. The applicable System of Records Notice is 09-20-0136, Epidemiologic Studies and Surveillance of Disease Problems.

The following PII will be collected CDC will use this information to maintain communications with respondents and to send respondents their results letters.

Name
Home Address (if study days will be at their home)

Workplace Address (if study days will be at their workplace)
E-mail
Telephone number(s)
Date of birth
Biologic specimens

The study staff will make every effort to keep the data secure by a variety of methods. Data are entered into a password-protected database. A unique Study ID is assigned as a key identifier for all study forms. The environmental and biological samples and measurements are only identified by study ID. Data collectors maintain their paper files in locked cabinets and their electronic files are stored on secured servers with password protection. Encrypted data files are sent electronically to investigators at CDC. Data are stored on highly-secured CDC servers in Atlanta, GA. The servers are housed in a secure computer room complete with climate control, emergency power, and an uninterruptible power supply (UPS). Daily back-ups and integrated security are implemented through the CDC computer services infrastructure. All data access is password-protected, and all network communications use encryption. All servers and PCs that are part of the CDC infrastructure are protected by both host-based firewalls and software in order to prevent the undetected installation of "spyware." At CDC, only our investigators are given access to read the encrypted data files.

Data are treated in a secure manner and are not disclosed, unless otherwise compelled by law.

Information about the data to be collected is below and summarized in Table A.10.1.

**Note:**

- **Cyanobacterial toxins = anatoxin-a, BMAA, cylindrospermopsin, nodularins, microcystins, and saxitoxin**
- **Liver enzyme levels = aspartase aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT)**
- **Gases and vapors emitted as cyanobacterial blooms die off = methane, ammonia, hydrogen sulfide, geosmin, methylisoborneal**

Environmental samples for each study day for each participant

- Air sampler on shore for aerosol particle size distribution and cyanobacterial toxin concentrations
- Air sampler on-shore for gases and vapors emitted as cyanobacterial blooms die off
- Personal air samplers for cyanobacterial toxin concentrations

Human biomonitoring specimens

- All study days (morning and evening)
    - Urine specimen for cyanobacterial toxin levels

    - Lung function test
    - Nasal swab for cyanobacterial toxin levels
    - Survey responses for activities and symptoms
- Study days 1, 3, and 5
    - Blood specimen for liver enzyme levels and creatinine levels

Fish biomonitoring

- Fish tested by EPA for cyanobacterial toxin levels

Other information

- Record of time spent outdoors

**Table A.10.1. 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 (see also SSB, Table B.2.1 and Consent form [Attachment 6]).**

| **Information & materials to be collected** | **Collected by** | **Number of times information and materials collected per participant**<br>**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 (morning and evening of each study day) | 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 cyanotoxin levels |
| Personal air samples | Study staff | 5 (one for each study day) | Cyanotoxin levels |
| Water samples | Study staff | 5 (one for each study day) | Cyanobacterial taxonomy and cyanotoxin levels |
| Nasal swabs | Study staff | 10 (morning and evening of each study day) | Cyanotoxin levels |
| Lung function test | Study staff | 10 (morning and evening of each study day) | Lung function parameters |
| Blood samples | Registered phlebotomist | 3 (on study days 1, 3, and 5) | Liver enzyme levels, creatinine levels |
| Urine samples | Study participants | 10 (morning and evening of each study day) | Cyanotoxin levels |
| Fish | Study staff (who will forward to EPA) | ≤5 (maximum of one for each study day when respondent is fishing) | Cyanotoxin levels in fish |

| | | | |
|---|---|---|---|
| Record of time spent outdoors | Study participants | 5 (one on each study day) | Hours spent outdoors |

We will post study Flyers (Attachment 4 – Flyer) throughout the community experiencing a cyanobacterial bloom to recruit potential respondents. The study Screening/Baseline Survey is Attachment 5, the Consent Form is Attachment 6, and the Symptom Survey is Attachment 7. Instructions for providing a blood specimen; for providing urine, nasal swabs, and lung function tests; and to be outfitted with a personal air sampler are in Attachments 8, 9, and 10, respectively. The Record of Time Spent Outdoors and Information about collecting a fish are in Attachments 11 and 12, respectively.

For the Screening/Baseline Survey, there are up to 33 questions, depending on the skip pattern applied. For the Symptom Survey, there are 51 questions pre- and 49 questions at the end of the study day (see Table A.10.3).

**Table A.10.2.** Overview of questions types in the Screening/Baseline Survey.

| Question Type | # of Questions Used |
|---|---|
| Name, home address (if relevant), workplace address (if relevant), email, phone numbers (to maintain contact during study, to allow us to go to their home or workplace, and provide individual results and final paper to respondents) | 3 |
| Demographics (age, sex, race—needed to interpret creatinine levels and lung function tests) | 2 |
| Occupation (to verify exposure potential) | 1 |
| Question about being outdoors for at least 2 hours per day | 1 |
| Question about ability to do a lung function test | 1 |
| Questions about other sources of exposure to cyanobacterial toxins (to use in assessing effects from exposure to Lake Okeechobee cyanobacterial blooms). | 2 |
| Diagnosis with asthma and/or COPD (Questions were used in previously OMB-approved national studies such as Behavioral Risk Factor Surveillance System [BRFSS]) | 1-11* |
| Diagnosis with other chronic conditions that may impact clinical test results (Based on the literature and professional judgement) | 3 |
| Alcohol use (recommended to help distinguish non-alcoholic liver injury associated with exposure to microcystins) | 1-2 |
| Smoking (recommended to help interpret lung function test results) | 1-3 |
| Use of blue-green algae supplements (to help evaluate exposures) | 1 |

| | |
|---|---|
| Water consumption (recommended to help interpret creatinine values) | 1 |
| Height and weight (needed to interpret lung function tests) | 2 |

* Total number of questions depends on responses.

**Table A.10.3.** Overview of question types in the survey.

| Question Type | # of Questions Used |
|---|---|
| Morning | |
| Questions about current respiratory and gastrointestinal illness | 2 |
| Symptoms possibly associated with exposure to cyanobacteria | 43 |
| Information about pet health | 6 |
| Evening | |
| Water quality | 5 |
| Symptoms of others | 1 |
| Symptoms possibly associated with exposure to cyanobacteria | 43 |
| Information about the species of fish and where it was caught | 2 |

For the survey, most questions are yes/no responses or multiple choice, except the three questions about pulmonary function testing results asked in the morning and evening.

We will provide study respondents with the results from their clinical assays (Attachment 13 – Results Letter).

Information about protection of privacy (i.e., the Privacy Impact Assessment) is in Attachment 14 – Privacy Impact Assessment.

Study documents will be maintained according to Records Control Schedule CDC RG-0442, Scientific and Research Project Records, Minor Research Records Authorized Disposition: Maintain at lease six years, but no longer than ten years after retirement of the system depending on the program needs for scientific, legal or business reference, then delete/destroy.

# A.11. Institutional Review Board (IRB) and Justification for Sensitive Questions

This study was reviewed by the NCEH/ATSDR human subjects advisor and determined to be non-exempt human subjects' research under 45 CFR 46. The CDC IRB approval memo is found in Attachment 15 – IRB Approval Memo.

CDC will not collect sensitive information from study respondents. CDC will collect age, race, and ethnicity data (see Attachment 5 – Screening/Baseline Survey) because it is needed to compare clinical test results with laboratory and other standards (e.g., lung function tests).

During the consent process, CDC-trained interviewers explain to the residents that participation in the study is voluntary and they may withdraw from the study at any time without negative consequences. The interviewers also explain the intended uses of the data, with whom information will be shared, and the legal authority for the data collection (i.e., through the Public Health Service Act). The interviewers will also ask if respondents are willing to be contacted for possible participation in future studies.

# A.12. Estimates of Annualized Burden Hours and Costs

The estimate of the burden of the information collection on respondents is displayed in Table A.12.1. The burden estimates for providing biomonitoring data were derived from CDC staff's experience in previous studies. Estimates for the time needed to complete the Screening/Baseline Survey and Symptom Survey are based on pilot testing with 7 volunteers.

**Table A.12.1 Estimates of annualized burden hours.**

| Type of Respondents | Form Name | Number of Respondents | Number of Responses per Respondent | Average Burden per Response (in hours) | Total Burden (in hours) |
|---|---|---|---|---|---|
| Interested community members | Screening/ Baseline Survey | 84 | 1 | 15/60 | 21 |
| Eligible study respondents | Symptom Survey | 67 | 10 | 15/60 | 167 |
| Eligible study respondents | Record of Time Spent Outdoors | 67 | 5 | 10/60 | 56 |
| Eligible respondents | Provide Blood Specimen | 67 | 3 | 15/60 | 51 |
| Eligible respondents | Provide Specimens | 67 | 10 | 1 | 670 |

| | | | | | |
|---|---|---|---|---|---|
| | (urine, nasal swabs, lung function test) | | | | |
| Eligible respondents | Be Outfitted with Personal Air sampler | 67 | 5 | 45/60 | 252 |
| Eligible respondents | Provide Fish (if respondent went fishing and caught fish) | 67 | 5 | 10/60 | 56 |
| Total | | | | | 1,273 |

Annualized cost to respondents for the burden hours for the collection of information is $31,050.00 and is provided in Table A.12.2. The mean hourly wage rate was obtained from the Department of Labor National Occupational Employment and Wage Estimates United States website (U.S. Department of Labor, Bureau of Labor Statistics, May 2018 National Occupational Employment and Wage Estimates, United States (https://www.bls.gov/oes/current/oes_nat.htm#45-0000). We used $24.42, the wage for first line supervisors of farming, fishing, and forestry workers as those workers are likely respondents.

**Table A.12.2. Estimated Annualized Burden Costs**

| Type of Respondent | Form Name | No. of Respondents | No. of Responses per Respondent | Average Burden per Response (in hours) | Total Burden Hours | Hourly Wage Rate | Total Respondent Costs |
|---|---|---|---|---|---|---|---|
| Interested community members | Screening / Baseline Survey | 84 | 1 | 15/60 | 21 | $24.42 | $513 |
| Eligible respondents | Symptom Survey and | 67 | 10 | 15/60 | 167 | $24.42 | $4079 |
| Eligible respondents | Record of Time Spent | 67 | 5 | 10/60 | 56 | $24.42 | $1368 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Outdoors | | | | | | |
| Eligible respondents | Provide Blood Specimen | 67 | 3 | 15/60 | 51 | $24.42 | $1228 |
| Eligible respondents | Provide Specimens (urine, nasal swabs, lung function test) | 67 | 10 | 60/60 | 670 | $24.42 | $16362 |
| Eligible respondents | Be Outfitted with Personal Air sampler | 67 | 5 | 45/60 | 252 | $24.42 | $6136 |
| Eligible respondents | Provide Fish (if respondent went fishing) | 67 | 5 | 10/60 | 56 | $24.42 | $1364 |
| Total | | | | | | | $31050 |

# A.13. Estimates of Other Total Annual Cost Burden to Respondents and Record Keepers

There are no additional costs to respondents.

# A.14. Annualized Cost to the Federal Government

The estimated annualized cost to the Federal Government over the three years of this OMB approval is detailed in Table A.13.1. The calculations are based on hours and estimates of the costs of sample collection, shipping and analysis from laboratory quotes.

**Table A.14.1. Annualized cost to the federal government.**

| Item | Total cost over three years | Annualized cost |
|---|---|---|

| | | |
|---|---|---|
| **Contract** | | |
| Personnel (including fringe) (680 hours) | $79,701.80 | $26567.27 |
| Travel | $33,600 | $11,200 |
| Consultant | $44,000 | $14,666.67 |
| Incentives | $30,750 | $10,250 |
| Equipment, sample collection, shipping, and analyses | $234,900 | $78,300 |
| Contract Subtotal | **$422,951.80** | **$140,983.94** |
| **Personnel** | | |
| PI (GS 15) 20% time (including fringe) | $120,960 | $40,320 |
| Study manager (GS 13) 50% of time (including fringe) | $180,000 | $60,000 |
| **Travel** | $33,600 | $11,200 |
| **TOTAL** | **$757,511.80** | **252,503.94** |

# A.15. Explanation for Program Changes or Adjustments

This is a new information collection.

# A.16. Plans for Tabulation and Publication and Project Time Schedule

The plans for tabulation and publication and project time schedule are detailed in Table A.16.1. Note that the time schedule for the activities are dependent on the development of a cyanobacterial bloom in Lake Okeechobee and the schedule may shift.

Table A.16.1 Project Time Schedule

| **Activity** | **Time Schedule** |
|---|---|
| Respondent recruitment | 1—2 months after OMB approval |
| Baseline information/data collection | 2—3 months after OMB approval |
| Information/Data collection | 3—8 months after OMB approval |
| Complete field work | 8—20 months after OMB approval* |
| Validation | 10—22 months after OMB approval* |
| Analyses | 12—30 months after OMB approval* |
| Publication | 30 months after OMB approval* |

* Timeline will be adjusted based on development of cyanobacterial bloom

## A.17. Reason(s) Display of OMB Expiration Date is Inappropriate

The display of the OMB expiration date is appropriate.

## A.18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification. These activities comply with the requirements in 5 CFR 1320.9.

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