Information Collection Request

Supporting Statement
Part A

Human Exposure to Cyanobacterial Toxins in Water
OMB No. 0920-0527
Reinstatement with Change

August 29, 2007

Project Officer:

Lorraine C. Backer, Ph.D, M.P.H.
Senior Environmental Epidemiologist
National Center for Environmental Health
Centers for Disease Control and Prevention
4770 Buford Highway NE
MS F-46
Chamblee, Georgia 30341
Phone: 770-488-3426
Fax: 770-488-3450
Lfb9@cdc.gov

A. JUSTIFICATION

A.1 Circumstances Making the Collection of Information Necessary

Cyanobacteria (blue-green algae) can be found in terrestrial, fresh, brackish, or marine water environments. Some species of cyanobacteria produce toxins that may cause acute or chronic illnesses (including neurotoxicity, hepatotoxicity, and skin irritation) in humans and animals (including other mammals, fish, and birds). A number of human health effects, including gastroenteritis, respiratory effects, skin irritations, allergic responses, and liver damage, are associated with the ingestion of or contact with water containing cyanobacterial blooms. Although the balance of evidence, in conjunction with data from laboratory animal research, suggests that cyanobacterial toxins are responsible for a range of human health effects, there have been few epidemiologic studies of this association (Codd et al., 1997).

The reported routes of human exposure to cyanobacterial toxins include drinking water, eating contaminated food, skin contact, inhalation, and hemodialysis. As with many naturally-occurring toxins, cyanotoxins are heat resistant and thus are not destroyed by cooking or heating contaminated food or water (Falconer, 1993). Evidence of adverse human health events from exposure to these cyanobacterial blooms is primarily anecdotal, but continues to accumulate.

In a recent study of Florida jet-skiers, Dr. Ian Stewart (Stewart et al., 2006) found increases in some symptoms and in respiratory illnesses in people who had been jet-skiing in bloom-contaminated waters. However, the sample size for this study was small, and there were a number of issues regarding recruiting, etc. that could be addressed in a larger study. We have identified recreational lakes in a number of states, including California, Michigan, Ohio, New York, Vermont, Texas, and Florida that have historically had blue-green blooms, including those

with cyanobacteria that produce microcystins. We have maintained contacts in these states who provide information about developing blooms in recreational waters.

Preliminary study

During August 2006, we conducted our first study to assess exposure to microcystins in recreational waters with a bloom of *Microcystis aeruginosa*. We recruited 104 people who were planning to be involved in water-related recreational activities that would generate aerosols, such as boating, fishing, water skiing, and using personal water craft. Ninety seven people did their activities on Lake 1, which had a confirmed *M. aeruginosa* bloom, and 7 others did their activities on Lake 2, which had no bloom. Study participants completed a pre-activity questionnaire, a post-activity questionnaire, provided a 10-ml blood sample, and completed a telephone symptom survey 7-10 days after exposure. On the days of the study, we collected water and aerosol samples to assess concentrations of microcystins.

Below is a summary of the data collected for the preliminary study:

1. Lake water samples were analyzed for microcystins using an ELISA (limit of detection [LOD] 0.15 ug/L). We collected water samples from the lakes according to our protocol. The concentrations of microcystins in Lake 1 ranged from 2 to 5 ug/L and in Lake 2 were all below the limit of detection. When we designed the study, we back-calculated to determine that a person exposed to recreationally-generated aerosols from water containing 10 ug/L of microcystins should have levels of microcystins in their blood that we can measure using the ELISA. However, the microcystin concentrations were actually 2ug/L to 5ug/L, much lower than we anticipated based on data from the previous week. Thus, the recreational exposures were not likely high enough for us to quantify microcystins in blood samples.

2. Air samples collected using hi-volume, multi-stage air samplers were analyzed for microcystins using an ELISA. The LOD for the test ranged from 0.0015 to 0.0049 ng/m^3 for the different stages of the air sampler. Air concentrations of microcystins ranged from 0.23 ng/m^3 to 0.57 ng/m^3.

3. Serum concentrations of microcystins were analyzed using an ELISA (Envirologix QuantiPlate Kit) with and LOD of 0.147 ug/L. All of the blood samples were negative for microcystins (i.e., were below the LOD).

Current Study design

Please note that we plan to repeat this study two times in areas with higher concentrations of microcystins (> 20 ug/L) in recreational waters.

For each of the two studies, we will recruit 100 study participants who are at risk for swallowing water or inhaling spray (i.e., water skiers, jet skiers, people sailing small boats) and who would normally be doing these activities, even in the presence of a bloom. We may recruit people who train for organized swimming events (e.g., triathlons) in lakes. In addition, for each of the two studies, we will recruit 50 study participants from lakes with no blooms as a comparison group to assess the health effects associated with recreational activities on "clean" lakes. The 100 exposed participants and 50 unexposed participants comprise the total of 150 participants for each study.

The purpose of this study is to continue assessing the public health impact of exposure to the cyanobacterial toxins, microcystins, during recreational activities. We will examine the extent of human exposure to microcystins present in recreational waters and associated aerosols and whether serum levels of microcystins can be used as a biomarker of exposure.

Below is a summary of the data we will collect. Study participants will complete a pre-activity questionnaire, a post-activity questionnaire, provide a 10-ml blood sample, and complete a telephone symptom survey 7-10 days after exposure. Serum concentrations of microcystins will be analyzed using an ELISA (Envirologix QuantiPlate Kit) with and LOD of 0.147 ug/L.

On the days of the study, we will collect water and aerosol samples to assess concentrations of microcystins as follows:

1. Lake water samples will be analyzed for microcystins using an ELISA (limit of detection [LOD] 0.15 ug/L). We will collect water samples from the lakes according to our protocol.

2. Air samples will be collected using hi-volume, multi-stage air samplers will analyzed for microcystins using an ELISA. The LOD for the test ranges from 0.0015 to 0.0049 ng/m^3 for the different stages of the air sampler. Respondents who will be using a jet ski or boat (for sailing or for water skiing) will also be asked to take a personal air monitor with them. The LOD for the ELISA is 70 ppt.

The data collection authority for this study is Section 301 of the Public Health Service Act (42 USC 241) (see Attachment 1).

A.2 <u>Purpose and Use of the Information</u>

The purpose of this data collection is to continue assessing human exposure to microcystin in recreational waters. The study will focus on environmental and serum levels of microcystins (see Attachment 2).

The results from this study will be useful to the health agencies in any states where

seasonal or year-round blue-green algae blooms occur in recreational waters. Specifically, it will provide the first evidence that people may be measurably exposed to cyanobacterial toxins during recreational activities. If we verify measurable human exposure to these toxins, then public health officials can take appropriate action (e.g., posting signs, using public information messages) to reduce or eliminate the exposure.

A.3 Use of Improved Information Technology and Burden Reductions

This collection of information will not use electronic collection techniques (i.e., a computerized questionnaire). The study instruments require collection of only the minimum information necessary for the purposes of the project.

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

An extensive review of scientific literature was conducted to locate other studies of people exposed to low levels of microcystins in recreational waters. The work by Ian Stewart (personal communication; Stewart et al., 2006) and our experience in August 2006 has provided a basis for collecting this new data. We could not locate any other study that assesses the association between recreational exposure to microcystins and subsequent quantitative and qualitative measures of microcystins in blood. In addition, communication with experts in environmental exposures did not bring to light any similar data collection efforts.

A.5 Impact on Small Business or Other Small Entities

No small businesses will be involved in this study.

A.6 Consequences of Collecting the Information Less Frequently

This is a data collection that will recur to verify results. There are no legal obstacles to reduce the burden of this data collection.

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

There are no special circumstances associated with this data collection. The data collection complies with the guidelines of 5 CFR 1320.5.

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

A. The notice of proposed data collection was published in the Federal Register on 2-12-07, Vol. 72, pages 6570-6571. The one public comment and our response are provided in Attachment 8.

B. The following individuals were consulted to obtain their views on the availability of data, the clarity of instructions, disclosure, and on the data elements to be recorded and reported.

Gregory Boyer (2001)
Faculty of Chemistry
State University of New York
College of Environmental Science and Forestry
Syracuse, New York 13210
Phone: 315-470-6825
Email: glboyer@esf.edu

Paul Berger (2000)
4607 - USEPA Headquarters
Ariel Rios Building

1200 Pennsylvania Avenue, NW
Washington, DC 20460
Phone: 202-260-3039
Email: berger.paul@epa.gov

Wayne Carmichael (2006)
Wright State University
221 Biological Sciences Building
Dayton, Ohio
Phone: 937-775-3173
Email: wcarmichael@desire.wright.edu

Michael Hodgson, MD, MPH (2000)
VHA (136)
810 Vermont Avenue NW
Washington, DC 20420
Phone: 202-273-8353
Email: muh7@mail.va.gov

Barbara Kirkpatrick (2006)
Mote Marine Laboratory
1600 Ken Thompson Parkway
Sarasota, Florida 34236
Phone: 941-388-4441
Email: bkirkpat@mote.org

Alan Rowan (2000)
Coordinator, Pesticide Exposure Surveillance Program
Florida Department of Health
4052 Bald Cypress Way, Bin A08
Tallahassee, Florida 32399-1712
Phone: 850-245-4117
Email: Alan_Rowan@doh.state.fl.us

Thomas Morris (2001)
Occupational and Environmental Epidemiology Branch
Harmful Algal Blooms Program
North Carolina Department of Health and Human Services
1912 Mail Service Center
Raleigh, NC 27699-1912
Phone: 919-715-2973
Email: thomas.morris@ncmail.net

James Sinclair (2000)

140
USEPA Facilities
26 West Martin Luther King Drive
Cincinnati, Ohio 45268
Phone: 513-569-7970
Email: sinclair.james@epa.gov

Steve Wiersma (2001)
Deputy State Epidemiologist
Florida Department of Health
2020 Capital Circle SE, Bin #A-12
Tallahassee, Florida 32399-1734
Phone: 850-922-9945
Email: steven_wiersma@doh.state.fl.us

Mark Vander Borgh (2001)
North Carolina Department of Environment and Natural Resources
Division of Water Quality
4401 Reedy Creek Rd
Raleigh NC 27607
Phone: 919-733-9960 ext 239
Fax: 919-733-9959
Email: mark.vanderborgh@ncmail.net

A.9 Explanation of Any Payment or Gift to Respondents

Study participants will receive a payment of $25 for participating in the study. This is consistent with our previous epidemiology studies that provide $5 for responding to short surveys, $10 for being available for follow-up phone surveys, and $10 for providing a blood sample.

A.10 Assurance of Confidentiality Provided to Respondents

This submission has been reviewed for Privacy Act applicability and it has been determined that the Privacy Act is applicable. The applicable Privacy Act system of records is 09-20-0136, "Epidemiologic Studies and Surveillance of Disease Problems." CDC has contracted with Mote Marine Laboratory to conduct study activities.

Identifying information such as name, address, and phone number will be collected, along with somewhat personal information regarding each individual's health history. Identifying information is necessary to facilitate the personal contact with respondents required to conduct the survey. Hard copies of questionnaires used for data entry at CDC will be identified by ID number only.

The paper documents containing personal identifiers will be kept in locked file cabinets at CDC and computer files will be password-protected and access will be limited to authorized study personnel. All staff working on the project will agree to safeguard the data and to not make unauthorized disclosures. Data will be safeguarded in accordance with applicable statutes. Responses in published reports will be presented in aggregate form and no individuals will be identified by name. See Attachment 4 for study participant Consent Forms.

45 CFR 46 (Regulations for Protection of Human Subjects) apply to this project. The protocol has been approved by the CDC Institutional Review Board (Attachment 5).

A.11 Justification for Sensitive Questions

Questions of a highly sensitive nature will not be asked, nor will social security numbers be requested. All respondents are told that participation in the study is voluntary and they may refuse to answer any of the questions.

A.12 Estimates of Annualized Burden Hours and Costs

A.12 - 1 Estimates of Annualized Burden Hour

The hour-burdens were estimated by testing the study instruments on fewer than 9 individuals who work at CDC. We anticipate doing two studies over the next three years. For the two studies, we anticipate that 376 people will do the screening questionnaire, 300 people will do consent forms, the post-exposure questionnaire, and the 10-day post-exposure questionnaire.

Table A.12-1

Forms	No. of Respondents	No. of Responses per Respondent	Avg. Burden per Response (in hours)	Total Burden Hrs.
Screening Questionnaire	125	1	5/60	10
Consent form(s) and Pre-exposure Questionnaire	100*	1	10/60	17
Post-exposure Questionnaire	100	1	15/60	25
10-day post-exposure Questionnaire	100	1	10/60	17
Total				69

*** Assuming an 80% response rate based on our previous field study**

A.12 - 2 Annualized Cost to Respondents

The hourly wage rate is $18.81 based on average weekly earnings in May 2005 from the Bureau of Labor Statistics web site at: http://www.bls.gov/oes/current/oes_nat.htm#b00-0000

Table A.12-2

Forms	No. of Respondents	No. of Responses per Respondent	Burden Hours	Hourly Wage	Total Respondent Cost
Screening Questionnaire	125	1	10	18.81	$ 188.10
Consent and Pre-exposure Questionnaire	100	1	17	18.81	$ 319.77
Post-exposure Questionnaire	100	1	25	18.81	$ 470.25
10-day post-exposure Questionnaire	100	1	17	18.81	$ 319.77
TOTAL					$1297.89

A.13 Estimates of Other Annualized Respondent Capital and Maintenance Costs

There are no other annualized respondent capital and maintenance costs.

A.14 Estimates of Annualized Cost to the Federal Government

Costs for CDC personnel were estimated based on experience with similar field studies.

Two field studies will be done over three years.

Table A.14

Item	Total Cost	Annualized Cost
CDC Personnel		
Salary	$ 35,000	$ 11,667
Fringe (20%)	$ 7,000	$ 2,333
Travel	$ 12,000	$ 4,000
Subtotal	**$ 54,000**	**$ 18,000**
Contracts		
Personnel		
On-site project director (2-times)	$ 5,000	$ 1,667
Plebotomist	$ 3,600	$ 1,200
Analytical Services	$56,800	$18,933
Reimbursements for participants	$ 7,500	$ 2,500
Subtotal	**$72,900**	**$24,300**
Supplies	**$ 2,600**	**$ 867**
Subtotal	**$129,500**	**$43,166**
CDC Administrative (15%)	$ 19,425	$ 6,475
Total	**$148,925**	**$ 49,642**

A.15 Explanation for Program Changes or Adjustments

Changes reflect our experience in conducting the first study of recreational exposures to microcystins. During August 2006, we conducted our first study to assess exposure to microcystins in recreational waters with a bloom of *Microcystis aeruginosa*. We recruited 104 people who gave informed consent to participate. Ninety seven people did their recreational activities on Lake 1, which had a confirmed *M. aeruginosa* bloom, and 7 others did their activities on Lake 2, which had no bloom. Study participants completed a pre-activity questionnaire, a post-activity questionnaire, provided a 10-ml blood sample, and completed a telephone symptom survey 7-10 days after exposure. The concentrations of microcystins in Lake 1 ranged from 2 to 5 ug/L and in Lake 2 were all below the limit of detection (LOD). When we designed the study, we calculated that a person exposed to recreationally-generated aerosols from water containing 10 ug/L of microcystins should have levels of microcystins in their blood. However, the microcystin concentrations in Lake 2 were below the LOD and in Lake 1 were actually 2ug/L to 5ug/L, much lower than we anticipated based on data from the previous week. Thus, the recreational exposures were not likely high enough for us to quantify microcystins in blood and the serum samples were all below the LOD for microcystins.

For the new data collection, we will conduct two separate studies in different lakes. In total we will recruit 200 study participants who are at risk for swallowing water or inhaling spray (i.e., water skiers, jet skiers, people sailing small boats) and who would normally be doing these activities, even in the presence of a bloom. We may recruit people who train for organized swimming events (e.g., triathlons) in lakes. In addition, we will recruit 50 study participants from lakes with no blooms as a comparison group to assess the health effects associated with

recreational activities on “clean” lakes. Study participants will be asked to sign a consent form, complete a symptom survey before and after doing their recreational water activities, provide one 10-ml whole blood sample after their recreational activities, and complete a telephone symptom survey 8-10 days after doing study activities.

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

Statistical Analysis Plan

We will collect blood samples (10 cc) from 150 participants ages 12 and older who agree to participate and who meet study criteria based on the screening questionnaire. The blood samples will be analyzed for levels of microcystins. Each participant will also be interviewed using a questionnaire containing questions on demographics and potentially confounding exposures.

Respondents who will be using a jet ski or boat (for sailing or for water skiing) will also be asked to take a personal air monitor with them.

We plan to compare the blood sample analyses from the two groups -- those swimming and playing in areas with a microcystins-producing bloom and those swimming and playing in an area without a microcystins-producing bloom. We will also assess the impact of potential confounders (e.g., use of blue-green algae food supplements) in evaluating exposure to microcystins.

A.16 - 1 Project Time Schedule

Table A.16-1

Activity	**Time Schedule**
Recreational water sample collection during a microcystins-producing bloom	After OMB approval (pending existence of a significant bloom)
Completion of field work	24-36 months after OMB approval (pending existence of a significant bloom)
Analyses	24-36 months after OMB approval
Publication	48 months after OMB approval

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

Exemption from displaying the expiration date for the OMB approval of forms is not being requested.

A.18 Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to certification for Paperwork Reduction Act Submissions.