Communities Organized to Prevent Arboviruses:

Assessment of Knowledge, Attitudes, and Vector Control Practices and Sero-Prevalence and Incidence of Arboviral Infection in Ponce, Puerto Rico (COPA Study)

Request for a Reinstatement
OMB No. 0920-1254
(Exp. 3/31/22)

Supporting Statement A

Program Contact

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- **Goal of the study:** To measure the incidence of arboviral infections in 38 communities in southern Puerto Rico.
- **Intended use of the resulting data:** The data obtained will inform decision making regarding the location, design, and content of future interventions to be implemented and evaluated to reduce the burden of arboviral disease in Puerto Rico.
- **Methods to be used to collect:** Longitudinal follow-up of a community cohort, annual sero-survey, cluster-randomized trial to evaluate the impact of the intervention.
- **The subpopulation to be studied:** All residents, 1–50 years old, from 38 selected clusters in Ponce are eligible. We aim to recruit 3,800 participants.
- **How data will be analyzed:** All statistical analysis will be conducted using SAS Version 9.4 and R Version 3.4.4. Descriptive analysis of all variables will be performed to examine the frequency and distribution of the data.

1. Circumstances Making the Collection of Information Necessary

This information collection request (ICR) is being submitted as a revision with an existing OMB number expiring on 03/31/2022. We are seeking three years of OMB clearance. This project was initiated in fall of 2017 by Ponce Health Sciences University (PHSU) in Ponce, Puerto Rico with the CDC Cooperative Agreement U01CK000580. Originally, CDC's role was limited to technical assistance including assisting with protocol development, advising on approaches to community-based interventions, vector control activities, diagnostic testing of enrolled patients, and data analysis. Since 2018, CDC's role has evolved to a point where CDC is co-leading this project.

The aim of this study is to establish longitudinal follow-up of a community cohort in communities in Southern Puerto Rico to measure the burden of arboviral infections and assess behaviors and perceptions related to arboviral disease and prevention. The study will also be used as a platform to investigate emerging health threats in the region, including novel coronavirus 2019 (COVID-19). The information collected will be used to inform public health officials on the implementation and evaluation of mosquito control interventions and other efforts to reduce the burden of arboviruses and other emerging diseases.

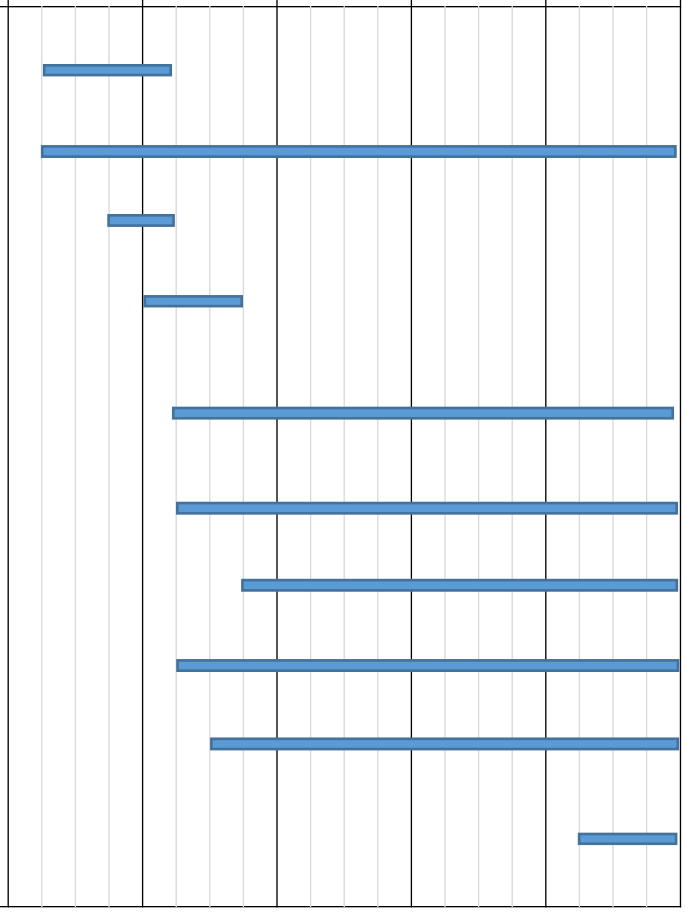
COPA progress report

The Communities Organized to Prevent Arboviruses (COPA) cohort has completed Year 1 and Year 2 activities and is currently in its third year with 68% participant retention. Seropositivity of IgM antibodies against dengue virus (DENV) in COPA for Year 2 was 0.4% and preliminary results from for Year 3 show the same level of seropositivity. There have not been any acute DENV infections detected in the cohort based on DENV RT-PCR test results since the study began. A collaboration with National Institute of Health (NIH) allowed for the completion of an analysis of DENV seroprevalence data among children enrolled in the COPA cohort, which has been used extensively to inform dengue vaccine recommendations and cost effectiveness models.

Data on acceptability of *Wolbachia* suppression, a novel vector control intervention involving releases of male mosquitos with *Wolbachia* bacteria, collected during Year 1 of the project showed that 64% of COPA participants supported the implementation of this intervention in their communities. The information collected on acceptability allowed project collaborators to design and implement a comprehensive communications plan before the implementation of the *Wolbachia* suppression intervention. The intervention was implemented as part of the cluster randomized trial started in September 2020, with releases of male *Aedes aegypti* mosquitoes with *Wolbachia* in 19 of the 38 study clusters. No sizeable decreases in the mosquito population were observed in the intervention clusters after 2 months of releases, and there were concerns about the number of mosquitoes released not being enough to suppress the wild population. In January 2021, the intervention clusters were reduced to 4 clusters (with 4 other clusters designated as control clusters) with the plan of extending to more clusters once suppression was achieved. We are currently monitoring the impact of this modified strategy.

All milestones from our last approval have been accomplished except for the ongoing evaluation of the impact of the intervention. The Acute Febrile Illness (AFI) surveillance (now Acute Illness Surveillance [AIS]) will be added to this OMB revision and implemented when it is approved.

MILESTONE	FY2018	FY2019	FY2020	FY2021	FY2022
• Complete baseline recruitment[*†]					
• Lab testing human and vector[† §]					
• Confirm intervention [*†§]					
• Obtain EPA permit for Puerto Rico[§]					
• Broad educational campaign[*†§]					
• Industry partnership[*§]					
• Deploy intervention[§]					
• Cohort follow up[*†]					
• Continuous AFI surveillance[*†]					
• Evaluation of intervention impact[*†§]					



* Supported by PHSU
†Supported by CDC
§Supported by PRVCU

The four viruses that cause dengue are transmitted by Aedes species mosquitoes and were introduced to the Americas over the past several hundred years where they have since become endemic. Puerto Rico, a Caribbean Island and U.S. commonwealth, has the highest burden of dengue virus in the U.S., and recent years have seen the emergence of two epidemic arthropod-borne viruses (arboviruses) also transmitted by Aedes mosquitoes. Chikungunya virus was introduced into the Caribbean in late 2013 and caused large epidemics of fever with severe joint pain throughout the Caribbean and Americas in 2014. Zika virus, the first arbovirus that can also be transmitted through sexual contact, was first detected in the Americas in 2014 and has been associated with devastating birth defects and Guillain-Barre syndrome. Yellow fever virus has recently caused large outbreaks in Brazil, and there is risk of importation to Puerto Rico and other counties in the Americas.

The public health response to the spread of these arboviruses throughout the tropics—where their mosquito vectors thrive—has been hampered by a lack of sustainable and effective interventions to prevent infection with any of these arboviruses at the community level. Moreover, the rapid speed with which new arboviruses spread does not often provide the time needed to plan and implement community-level interventions to decrease disease transmission. Although several candidate vaccines for chikungunya and Zika viruses are currently in clinical development, none are yet available. A dengue vaccine was recently recommended for children 9-16 years old with previous dengue infection and living in dengue-endemic parts of the United States. However, this will only benefit a small proportion of the population at risk for dengue infection.

Among the newer approaches to minimize mosquito-borne transmission of pathogens that cause human disease is the release of mosquitoes infected with a strain of the bacteria called *Wolbachia*. *Aedes (Ae.) aegypti* is one of a few mosquito species not naturally infected with *Wolbachia*, and infection with *Wolbachia* tends to block transmission of dengue, chikungunya, and Zika viruses from these mosquitoes. *Wolbachia* replacement, which involves the replacement of wild *Ae. aegypti* populations with *Wolbachia* infected mosquitoes, is currently being evaluated as an approach to reduce arboviral infections in large trials in southeast Asia, Colombia, and Brazil. This approach has not been used in the United States. Another potential approach known as *Wolbachia* suppression prevents reproduction of mosquitoes by introducing a strain of *Wolbachia* bacteria into males that results in sterile eggs from all mating due to an effect known as cytoplasmic incompatibility. The release of large numbers of sterile male insects has been used for agricultural pests with success, such as for screwworm in Central America and tsetse flies in Zanzibar. In the United States, *Wolbachia*-infected *Ae. aegypti* mosquitoes can be used for vector control under a location-specific Environmental Protection Agency (EPA) Experimental Use Permit (EUP). Field trials of these mosquitoes are underway to provide data to complete EPA's registration process.

A vital part of community-based vector control programs is an investigation of local perceptions of disease and health, the control and prevention of disease, and behavior related to the use of health services. Community perceptions obtained from surveys can then be incorporated into vector control strategies.

The law/regulation requiring that CDC collect the info: Authorizing Legislation comes from Section 301 of the Public Health Service Act (42 U.S.C. 241). (Attachment 1)

2. Purpose and Use of Information Collection

The aim of this study is to establish longitudinal follow-up of a community cohort in several communities in southern Puerto Rico and evaluate community acceptance and impact of a novel vector control intervention. The study will evaluate whether the intervention leads to a reduction in *Ae. aegypti* population and a measurable decrease in the incidence of arboviral infection among people in intervention clusters compared to those in non-intervention clusters. The information from this project will be used to inform public health officials about challenges, impact, and acceptability of vector control interventions to better plan and implement such interventions in Puerto Rico. The

original plan is to conduct this study for five years, including three years of follow-up once the intervention is implemented. The duration of the project could be expanded depending on support and funding availability.

The general aims of the COPA project are:

AIM 1

Conduct a cluster randomized trial to evaluate the impact of a novel vector control strategy in selected areas in Ponce Puerto Rico.

a. Establish a community cohort to conduct surveillance for arboviral infections in the selected clusters in Ponce, Puerto Rico and follow participants longitudinally.
b. Evaluate the prevalence and annual incidence of arboviral infections in participating areas in Ponce using molecular and serological tests.
c. Evaluate overall health status, mental health, comorbidities, alcohol and drug use, access to health care, knowledge, attitudes, and practices on vector control, and human mobility patterns in the selected clusters.
d. Coordinate the implementation of the intervention with the vector control unit in intervention areas.

AIM 2

Define the clusters selected for participation and understand local needs to adapt and customize vector control strategies.

a. Evaluate how the cluster is organized and identify community leaders and main stakeholders.
b. Identify main health concerns, health seeking behavior, and health facilities utilized.
c. Describe cluster attitudes and acceptability towards current and novel vector control strategies.
d. Identify the best strategies to get buy-in for proposed vector control strategies from community leaders, stakeholders and community members.
e. Investigate the main barriers and facilitators to implement vector control strategies.
f. Describe what communities consider is their role, the government's role, and other stakeholders' role in mosquito control.

AIM 3

Establish ongoing entomological surveillance for *Ae. aegypti* in selected clusters.

a. Measure adult mosquito populations through the use of autocidal gravid ovitraps (AGOs).
b. Conduct an environmental survey to assess potential breeding sites.

AIM 4

Establish a surveillance system to assess annual incidence of acute febrile illness and evaluate its etiology among cohort participants.

a. Evaluate the number of persons with AFI and the number seeking care.
b. Implement participatory surveillance through mobile phone and computer technology.

c. Evaluate the incidence and etiology of non-arboviral acute febrile illness among study participants (separate protocol on banked specimens).

The Puerto Rico Vector Control Unit (PRVCU) was formed as part of a cooperative agreement between the CDC and the Puerto Rico Science, Technology and Research Trust in late 2016. The PRVCU's objectives include establishing surveillance and control of mosquito vectors in Puerto Rico, specifically *Ae. aegypti*. The PRVCU was tasked by the Governor's Executive Order No. OE-2016-037 with overseeing and implementing vector control activities in Puerto Rico in collaboration with other Puerto Rico agencies including the Puerto Rico Health Department and the Puerto Rico Department of Agriculture. The goal of the program is to impact the *Ae. aegypti* population sufficiently to prevent virus transmission to humans and reduce morbidity and mortality associated with vector-borne diseases.

They are responsible for two components of the COPA project, the implementation of mosquito surveillance and the implementation of the vector control intervention. Since April 1, 2018, PRVCU has been progressively installing autocidal gravid ovitraps (AGOs) for surveillance of adult female *Aedes aegypti* mosquitoes in the 38 clusters. PRVCU has placed traps at a density of 1 trap per 250 square meters across clusters. PRVCU staff carries out mosquito identification counting on a weekly basis.

The selection of the intervention is based on several considerations including: 1) Recommendations from WHO on which intervention is ready for large-scale field trials; 2) EPA regulatory requirements and 3) Community support. In order to determine which intervention to use, the PRVCU conducted consultations with different sectors from the Puerto Rico public and scientific community. The intervention with the highest level of support has been Wolbachia suppression. In support of PRVCU findings, preliminary data from the COPA baseline survey found 70% of participants support the release of non-biting male mosquitoes as an environmentally neutral biological control. We expect this high acceptance level to increase after educational campaigns detailing this vector control strategy. The use of *Wolbachia* to control *Aedes* spp. populations and arboviral disease transmission is regulated by the U.S. Environmental Protection Agency under an Experimental Use Permit. The Puerto Rico Secretary of Health has given preliminary approval for the use of *Wolbachia* suppression. We expect endorsement from the leadership advisory board of the Puerto Rico Vector Control Unit (PRVCU) in early May 2019. Based on the regulatory approvals and community support Wolbachia suppression has been chosen as the intervention. Half of the clusters will receive the intervention and half will serve as controls. The baseline assessment will take two years. Follow-up after the intervention is implemented will be 3 years.

To assess acceptability of traditional and novel vector control interventions, a questionnaire including a brief description of several interventions and the level of opposition/support for each of them will be administered to approximately 50% of adult participants. This information is important to establishing which interventions are more likely to be acceptable to cluster residents. Preliminary results for the baseline were used to inform the selection of the intervention. We wanted to document the level of support and identify areas for additional community education. Participants are asked to explain reason(s) for opposition when applicable, providing valuable information on concerns and misconceptions that can be used to inform future educational campaigns and community activities.

The collection of information will be done through a questionnaire covering demographics, vector control, healthcare seeking behavior and other areas discussed below. We will collect demographic information (e.g., age, sex, duration of time residing in Puerto Rico), travel history, and information on recent illnesses from all participants via household (and individual) questionnaires. The questionnaires will be administered after written consent and written or verbal assent (for minors) from those present in the household at the time of the visit. GPS coordinates will also be collected for each household visited to later assess for potential clustering of arboviral infections within communities. We will ask participants if they have been ill with arbovirus- or COVID-19-like illness (i.e., fever, rash, fever, cough, sore throat, difficulty breathing, diarrhea, body pain, or loss of taste/smell in the last week) in the past week and year. If so, we will collect details on the symptoms experienced during their illness. The survey incorporated observations from focus group discussions and cognitive testing.

At the time of survey administration, ~15 mL of blood will be collected to conduct serologic diagnostic testing for arboviruses.

An acute illness surveillance (AIS) project component is being implemented to better identify and assess the incidence of arboviral disease and COVID-19 among COPA participants. This additional weekly activity will use an **automated text-messaging system** to ask COPA household representatives and other household adults who consent to receive text messages if any COPA participants in the household have experienced fever or other COVID-like symptoms in the past 7 days. Project staff will contact households in which one or more participants reported symptoms to schedule an appointment to collect samples for arbovirus and SARS-CoV-2 molecular testing and to administer a **AIS questionnaire** about symptoms, exposure and health seeking behaviors. From previous febrile surveillance studies, we expect approximately 40% of household adults will respond to text messages each week and 10% of COPA participants will report acute symptoms and agree to a sample collection visit each year.
Participants with a positive SARS-CoV-2 molecular test will be contacted by phone 2-4 weeks later for a **COVID-19 case follow-up questionnaire** on symptoms, health care seeking, potential exposures, and outcomes of SARS-CoV-2 infection. We are expecting that 20% of participant that report symptoms will have a positive COVID-19 result and respond to this follow-up questionnaire.

Specific information collection instruments include:

These questionnaires will be administered to all COPA participants, of the selected clusters in Ponce. Being a resident is defined by having slept in the house for at least four of the past seven nights and not having plans to move in the next year. The questionnaire sections will vary depending on the age of each participant.

Eligibility and consent information (Attachment 2).

Household representative questionnaire (Attachment 3) This questionnaire will be administered to one household representative in each home with one or more participants. This representative should be 21 years or older or an emancipated minor. If all eligible household members are un-emancipated minors, a household member over the age of 50 may act as household representative and complete this section of the survey only. A minor residing without an adult in the household may participate and act as a household representative if they have parent or legal guardian consent to do so. This

information is key to ensure follow-up of the cohort, to understand the household composition, household income, frequency and type chemical insecticide, and contact information. It will also be used to identify sub-groups at higher risk of arboviral infection.

Individual questionnaire (Attachment 3), to be administered to all participants to collect individual-level socio-demographic information. This section will provide information on past illnesses and health seeking behaviors. It will be used to identify the main healthcare facilities used in the area, and costs associated with acute febrile illness. We will ask participants if they have been ill with arbovirus-like illness (i.e., fever, rash, joint pain, and conjunctivitis) in the past year. If so, we will collect details on the symptoms experienced during their illness. Questions related to COVID-19 vaccine uptake, illness, and diagnosis are also included to describe and estimate the number of previous SARS-CoV-2 infections and evaluate the success of ongoing COVID-19 vaccination efforts in these communities.

Knowledge, attitudes, and practices questionnaire (Attachment 3) This questionnaire will be administered to participants 14-50 years old to collect information on knowledge, perceptions of risk and prevention measures, and past experience with dengue and COVID-19. This data will be used to understand how community members view arboviral diseases and COVID-19 and how these perceptions relate to experience and willingness to adopt individual and community-level prevention measures. Questions related to general perceptions and confidence in vaccines will be asked to see how these relate to intentions to vaccinate against dengue and COVID-19. The questionnaire will also be focused on vector control and dengue vaccine intention and uptake. This information will be used to identify factors associated with higher risk of arbovirus infections and to inform development and roll-out of dengue vaccines on the island.

Specimen information (Attachment 3) At the time of the questionnaire administration, ~15 mL of blood will be collected to conduct serological testing of arboviruses for a sero-survey. This form is used to identify and track specimens.

Mobility questionnaire (Attachment 3) will be administered to all participants to assess general individual-level mobility patterns, including time spent in and outside of the home each week. We will ask participants about the location and characteristics of places where they spend more than 5 hours a week to assess potential arboviral exposures outside of the home.

Vector control intervention questionnaire (Attachment 3), to be administered to the household representative. This section will be used to assess acceptability of traditional and novel vector control interventions. This information is important to establishing which interventions are more likely to be acceptable to cluster residents. Participants are asked to explain reason(s) for opposition when applicable, providing valuable information on concerns and misconceptions that can be used to inform future educational campaigns and community activities.

Automated text-messaging system (Attachment 3) Will be sent to ask COPA household representatives and other household adults who consent to receive text messages if any COPA participants in the household have experienced fever or other COVID-like symptoms in the past 7 days.

AIS questionnaire (Attachment 3) This questionnaire will be administered to all participants that reported symptoms and agreed to provide a nasal sample, it will provide information about symptoms, exposure and health seeking behaviors.

COVID-19 case follow-up questionnaire (Attachment 3) This questionnaire will be administered to all participants with a positive SARS-CoV-2 molecular test that agree to provide a nasal sample. They will be contacted by phone 2-4 weeks after their AIS positive sample. The questionnaire will provide information on symptoms, health care seeking, potential exposures, and outcomes of SARS-CoV-2 infection.

The central COPA questionnaires (Household, individual, KAP, mobility, Vector Control) will be repeated among approximately 3,800 participants every 12 months, up to a period of 5 years. The AIS and COVID-19 follow-up components will be renewed and modified annually as applicable according to research and funding priorities. OMB clearance will be extended after three years.

GPS coordinates will also be collected for each household visited to later assess for potential clustering of arboviral and COVID-19 infections within neighborhoods.

3. Use of Improved Information Technology and Burden Reduction

Collected data will be directly recorded in tablets to minimize data entry errors and minimize delays in data availability. If paper forms must be used, interview responses will be entered into the database either daily or as a group at the close of data collection Household structure ID numbers and locations will be loaded on to each tablet through an electronic household tracking tool app; structure IDs will also be pre-loaded into REDCap for consent and interview information. Questionnaire data will be directly entered into REDCap, a secure web application for building and managing online surveys and databases. In cases where data collection using electronic devices is not possible, participant responses will be collected on paper for later data entry in REDCap. Ten percent of entered forms will be re-checked to identify any problems with data entry accuracy that must be addressed. During the initial years of the project, Epi Info software was used for tablet-based data collection.

4. Efforts to Identify Duplication and Use of Similar Information

CDC is not aware of the availability of any similar information or ongoing projects within CDC or in other governmental agencies. Passive surveillance for arboviral diseases has many limitations, including the lack of long-term follow-up, frequency of asymptomatic infections, and sparse data collected. A longitudinal cohort provides the opportunity to gather this critical data to inform and evaluate dengue prevention and control measures and more accurately assess arboviral incidence and burden.

5. Impact on Small Businesses or Other Small Entities

This data collection will not involve small businesses.

6. Consequences of Collecting the Information Less Frequently

The questionnaires need to be administered annually to be able to provide a comparison of before and after vector control interventions, to detect the impact of an intervention and to increase the robustness of the scientific conclusions of the collection. The collected information will also help us understand the risk, perceptions, and burden of arboviral infections and COVID-19 and evaluate a community-based approach for vector control in 38 communities in Ponce, Puerto Rico. The information obtained will inform decision making regarding the location, design, content, and evaluation of future mosquito control interventions implemented in Puerto Rico. Data on incidence and perception of COVID-19 disease will also be used to inform local control programs and fill the current knowledge gaps.

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

This request fully complies with the regulation 5 CFR 1320.5.

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 November 22, 2021, vol. 086, No.222, pp. 66311-66313 (Attachment 4). CDC did not receive public comments related to this notice.

Efforts to consult outside the agency
Research collaboration with other federal agencies and academic institutions

National Institute of Health

To better understand and define the immune response to previous dengue and Zika virus infections, CDC is collaborating with the NIH in laboratory testing for the COPA project. Selected specimens from COPA participants will be shared with the laboratory of Dr. Stephen Whitehead for plaque reduction neutralization testing, which can identify neutralizing antibody responses for each dengue virus serotype and Zika virus. This testing answers critical questions about primary versus secondary infection by age and informs seroprevalence estimates for the population.

University of Florida

CDC has an ongoing collaboration with researchers at the University of Florida, who provide analytic support and technical consultations for the COPA project. Dr. Cummings and Dr. Hitchings conduct mathematical modeling to inform the design and monitoring of a cluster randomized trial to evaluate the epidemiological impact of a novel vector control intervention, which includes (1) Modeling dengue seroprevalence and incidence by age group in Ponce to determine the impact of the current age distribution of the cohort and provide data to evaluate our assumptions for the sample size calculations; (2) Modeling of IgG and IgM dynamics to determine how many incident infections will be identified in annual assessments; and 3) Using data from the previous serosurveys to understand how mobility (time spent outside the house) could reduce the protective impact of an intervention.

An external peer review with five experts in the field of arboviral disease and community engagement had the following assessment of the COPA project: “The COPA project is a good example of where the [Dengue] Branch has created opportunities to combine epidemiology, social and behavioral sciences, policy, clinical research, implementation research and modelling in ways that could provide unique insights into the design and performance of integrated vector control programs that could be extremely valuable for programs around the world.”

As part of the COVID-19 Emergency Response efforts to better understand and control the COVID-19 epidemic, CDC is overseeing design and implementation of cohort studies to investigate how SARS-CoV-2 spreads through households and community groups. The COPA project was identified by the COVID-19 Emergency Response Epidemiology Task Force as an existing study that could be expanded to meet COVID-19 investigation objectives. To that end, questions related to risk and perception of COVID-19 will be added to the annual questionnaire, an acute illness surveillance (AIS) component will be implemented to provide SARS-CoV-2 molecular testing for participants with acute COVID-like symptoms, and additional questionnaires will be applied to participants with acute symptoms and/or COVID-19 identified via molecular testing to gather data on illness characteristics, health care seeking behaviors, and potential exposures. The AIS component will also complement COPA annual sero-surveillance activities by providing molecular testing for arboviruses to participants with current or recent acute fever to identify incident and recent infections with dengue and other circulating arboviruses.

9. Explanation of Any Payment or Gift to Respondents

Participants will be provided with a token of appreciation of 30 dollars, when they agree to provide a blood sample for the study. The token of appreciation is given to the participant even if the blood draw is not successful. For participants under 7 years of age, the parent will receive the full token of appreciation.

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

CDC’s Information Systems Security Officer reviewed this submission and determined that the Privacy Act does apply. A Privacy Impact Assessment is included as part of this submission (Attachment 5). The applicable Systems of Records Notice is 09-20-0136, Epidemiologic Studies and Surveillance of Disease Problems.

Data collection and management

The COPA data collection and management system utilizes encrypted tablets, REDCap and R Shiny software, and encrypted file transport infrastructure and data storage within the CDC network. Data is currently being stored in a secure, limited access CDC network drive, which was implemented to store data containing PII. COPA data collection and management architecture was developed in compliance with federal data security guidelines and CDC’s Office of the Chief Information Security Officer (OCISO) policies and tools which have been reviewed and approved for collecting and managing data with PII.OCISO has granted an Authority-To-Develop, a designation to develop the COPA data system in a

SQL Server database environment. All DVBD developers will meet OCISO standards in the build-out and deployment of this system. COPA will seek the Authority-To-Operate, an OCISO designation for deployment, once the development of the more complex SQL based system is finalized.

Only interviewers and staff trained in specimen collection will be used in the proposed project. This project will collect and record personal identifying information (e.g., name, contact information, GPS coordinates of residence, picture of the residence). As in all studies involving human subjects, this project will involve people whose rights need to be safeguarded. A label with a project identifier will be placed on blood tubes and questionnaires and will be used to link all data collected during the project. All serum specimens will be securely transported to and stored at PHSU/PRI and CDC Dengue Branch labs. All data will be entered into a survey database that will be secure; only personnel on the investigation team will have access to it. All personnel involved in this project will be required to adhere to an unwavering code of conduct regarding the confidentiality of patients' information. Data will be kept as confidential as permitted by law. Hard copies of questionnaires will be stored in a room at PHSU/PRI that will be locked when not occupied. Based on human subject requirements, paper records will be kept for the duration of the study and at least three years after that. After this period, they will be archived or destroyed according to federal records management guidelines. Access to these files will be limited to project personnel. Electronic copies of the data will be kept in the above-mentioned database, which will be password protected and will only be accessible to relevant project personnel.

Project procedures and confidentiality protection procedures are outlined below:

- A randomly generated list of numbers will be produced that correspond to households from clusters.
- A list of COPA participants will be generated to provide follow up.
- Households will be visited and offered enrollment. Questionnaires and serum specimens will be collected from participating household members.
- Serum specimens will be received at CDC Dengue Branch and PHSU lab and assigned a numeric identifier that is distinct and unrelated (though traceable) to their identifying information, which will also be entered into the database along with information collected via questionnaires, which will also be entered into a secure database.
- Serum specimens will be tested by RT-PCR and IgM and IgG ELISA for evidence of current, recent, or historic CHIKV, ZIKV, and DENV infection, respectively.
- Test results will be sent to participants by mail or secure email by project staff.
- Data analysis will be performed using the coded, password protected electronic database.

Informed consent

The consent form includes authorization to participate in the project, to provide a blood sample, to house inspection, to contact the participants, to send lab results, invite them to informative meetings on vector control and other related topics, and inform them of annual follow-up activities.

We will use the consent summary (Attachment 6) to summarize the most important points of the informed consent to participants.

Consent/assent forms will be generated in English, translated to Spanish by a native Spanish speaker from Puerto Rico, and back-translated to English by a separate person to ensure accuracy. After the

participants complete consent and assent if required, project staff will give all patients a simple informational sheet about dengue, chikungunya, and Zika viruses.

Potential participants will also be informed on the consent forms that they should contact PHSU staff should they have any questions about their rights as a research subject.

Data will be stored at Ponce Health Sciences University and CDC's Dengue Branch; only members of the project will have access to the data. Participants' names, addresses and telephone numbers will be collected in case we need to contact them later in the project. This information will be kept secure in password protected computers and locked cabinets. Based on human subject requirements, paper records will be kept for the duration of the study and at least three years after that. After this period, they will be archived or destroyed according to federal records management guidelines.

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

Institutional Review Board (IRB)

NCEZID's Human Subjects Advisor has determined that information collection is research involving human subjects. IRB approval was required (Attachment 7).

CDC's Human Research Protection Office reviewed and approved the request to allow reliance on a non-CDC IRB for protocol #171110-VR "Communities Organized to Prevent Arboviruses: Assessment of Knowledge, Attitudes, and Vector Control Practices and Sero-Prevalence and Incidence of Arboviral Infection in Ponce, Puerto Rico" in accordance with 45 CFR 46.114. The protocol has been reviewed and approved by the Ponce Medical School Foundation - Ponce Research IRB for the maximum allowable period of twelve months and the IRB's approval will expire on 10/26/2022.

Justification for Sensitive Questions

Sensitive questions on mental health will be used to better understand co-morbidities, health-related risk factors, beliefs, and behaviors among study population. These conditions and behaviors have implications for health seeking behavior, arboviral disease outcomes as well as community engagement and education efforts. This study includes a strong component of community engagement to ensure acceptability of the intervention and participation in vector control activities. Understanding other potential health problems will help us tailor community activities and future educational campaigns.

12. Estimates of Annualized Burden Hours and Costs

A. Estimated Annualized Burden Hours

To arrive to the estimated annualized burden hours, we piloted the questionnaire with 10 community members. The total number of estimated annualized burden hours for this project is 4,349.

To meet recruitment goals, the Household Representative questionnaire will be completed once a year by approximately 2,700 participants. With a total desired sample of 3,800 participants, we expect the

number of household representatives to be around 2,700 considering that we need about 86 houses per cluster and one household representative per house. It will take an average of ten minutes to complete each Household Representative questionnaire for a total annual burden of 450 hours.

The Individual questionnaire will be completed once a year by all (~3,800 participants); it will take an average of 20 minutes to complete this questionnaire for a total annual burden of 1,267 hours. The estimated annual burden is an overestimation as there are several questions included that are only asked to participants of a specific age or to parents. Specimen collection will also be completed once a year by all participants. Based on data from previous years, it takes an average of 5 minutes to complete the specimen collection for a total annual burden of 317 hours. The Mobility questionnaire will be a completed once a year by all participants. It will take an average of 10 minutes to complete this questionnaire for a total annual burden of 633 hours. These three questionnaires will be merged into a single document for ease of administration.

The Knowledge, Attitudes, and Practices (KAP) questionnaire will be a completed once a year by 14 years and older (~3,090 participants based on number of participants ages 14 to 50 years recruited in previous years). It will take an average of 15 minutes to complete this questionnaire for a total annual burden of 773 hours. The estimated annual burden is also an overestimation as there are several questions included that are only asked to participants of a specific age or to parents.

The Vector Control questionnaire will be completed once a year by all participants 21 years or older (~2,500 participants based on number of participants age 21 to 50 years recruited in previous years). It will take an average of 10 minutes to complete this questionnaire for a total annual burden of 417 hours.

The AIS text message will be completed 52 times a year by participants who respond (~1,000 participants per week). Based on data from previous years, we have recruited ~ 2,500 participants ages 21 to 50, and these participants will receive the text messages. However, based on response rates from similar projects in the region, we expect only ~40% of these participants will respond to the text message each week. It will take an average of .5 minute to answer this text for a total annual burden of 433 hours.

The AIS questionnaire will be completed as needed when symptoms are reported (~ 380 participants based on the estimate that 10% of our 3,800 participants will report symptoms during a year). It will take an average of 8 minutes to complete this questionnaire for a total annual burden of 51 hours.

The COVID-19 Case Follow-Up questionnaire will be completed as needed by participants with a positive SARS-CoV-2 PCR test (~76 participants). We estimate that 20% of 380 participants reporting symptoms will have a positive SARS-CoV-2 test during a year. It will take an average of 6 minutes to complete this questionnaire for a total annual burden of 8 hours.

The breakdown of how this estimate was reached is in the following table.

Estimated Annualized Burden (Hours)

Type of Respondents	Form Name	No. of Respondents	No. of Responses per Respondent	Average Burden per Response (in hours)	Total Burden Hours
Ponce residents from the 38 selected communities 21 years and older or emancipated minor	Household Representative questionnaire	2,700	1	10/60	450
Ponce residents from the 38 selected communities 1- 50 years old	Individual† questionnaire	3,800*	1	20/60	1,267
Ponce residents from the 38 selected communities 1-50 years old	Specimen† collection	3,800	1	5/60	317
Ponce residents from the 38 selected communities 1- 50 years	Mobility† questionnaire	3,800	1	10/60	633
Ponce residents from the 38 selected communities 14 - 50 years old	Knowledge, Attitudes, and Practices (KAP) questionnaire	3,090*	1	15/60	773

Type of Respondents	Form Name	No. of Respondents	No. of Responses per Respondent	Average Burden per Response (in hours)	Total Burden Hours
Ponce residents from the 38 selected communities 21 years and older	Vector Control questionnaire	2,500	1	10/60	417
Ponce residents from the 38 selected communities 21 years and older	AIS text message	1,000	52	0.5/60	433
Ponce residents from the 38 selected communities with inclusion criteria	AIS questionnaire	380	1	8/60	51
Ponce residents from the 38 selected communities with inclusion criteria that tested positive for SARS-CoV-2	COVID-19 Case Follow-up questionnaire	75	1	6/60	8
Total					4,349

*Not all participants will answer all questions, burden is overestimated

†Will be merge into one document

B. Estimated Annualized Burden Costs

The average annual response burden cost is estimated to be $46,031. The hourly wage estimates are based on the minimum Puerto Rico wage ($8.50) approved for January 1st, 2022 by the Hon. Pedro Pierluisi, Governor of the Commonwealth of Puerto Rico.

Type of Respondent	Form Name	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Ponce Residents	Household Representative questionnaire	450	$8.50	$3,825
	Individual questionnaire	1,267	$8.50	$10,770
	Specimen collection	317	$8.50	$2,695
	Mobility questionnaire	633	$8.50	$5,381
	Knowledge, Attitudes, and Practices questionnaire	773	$8.50	$6,571
	Vector Control questionnaire	417	$8.50	$3,545
	AIS text message	433	$8.50	$3,681
	AIS questionnaire	51	$8.50	$434
	COVID-19 Case Follow-Up questionnaire	8	$8.50	$68
Total				$36,970

13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers

There are no costs to respondents other than their time.

14. Annualized Cost to the Government

The cost to the federal government is estimated at $2,073,176. The project will require four Epidemiologists (two full time and two 35% of their time), three Public Health Advisors (full time time), 2 Data Managers (one full time and one 50% of their time), two Fellows full time, one Communication Specialist (30% of their time), two Biostatisticians (20% of their time), one Behavioral Science Specialist (50% of their time), three Programmers (40% of their time), one Data Entry (full time), and 21 Ponce Health Science University employees, including but not limited to, Interviewers, Phlebotomists, and Principal Investigator full time. For CDC employees, hourly wage rates were used for the Puerto Rico

locality. These numbers are available at https://www.opm.gov/policy-data-oversight/pay-leave/salaries-wages/salary-tables/18Tables/html/RUS_h.aspx. CDC contracting employees' hourly wages were calculated from the government and contracting company contract. For PHSU employees, the hourly rate is an average of the total amount allocated in the Cooperative Agreement for the institution to hire employees.

Position	Hours	Average Hourly Wage	Total
Epidemiologists (x4)	5,720	$40.00	$228,800
PHAs (x3)	6,240	$48.72	$304,013
Fellows (x2)	4,160	$43.27	$180,003
Data Managers (x2)	3,120	$34.00	$106,080
Communication specialist (x1)	624	$30.00	$18,720
Biostatistician (x2)	832	$59.00	$34,786
Behavioral Science Specialist (x1)	1,040	$50.96	$52,998
Programmers (x3)	2,496	$58.00	$144,768
Data Entry (x1)	2,080	$28.85	$60,008
PHSU Cooperative Agreement employees (x21)	2,080	$21.59	$943,000
Total			$2,073,176

15. Explanation for Program Changes or Adjustments

Study sample size changes:

Cluster areas have been re-defined and new sample size calculations were performed to accommodate the PRVCU's selected vector control intervention approach (*Wolbachia* suppression), including cluster size, geography, and "buffer zone" between clusters needed for intervention. The 14 original cluster areas have been sub-divided and additional clusters were added for a total of 38 cluster/community areas (of 200 to 500 acres) with the aim of recruiting and maintaining 65 participants per cluster over a 3-year period to assess the PRVCU intervention impact on incidence of arboviral infections. To account for loss-to-follow-up and arbovirus seropositivity at baseline, we estimated that we need to enroll and maintain 3,800 participants (or approximately 100 participants per cluster) rather than the original estimate of 4,000 participants.

Questionnaire additions and changes:

As part of the COVID-19 Emergency Response efforts to better understand and control the SARS-CoV-2 epidemic, CDC identified the COPA study as an existing study that could be expanded to meet COVID-19 investigation objectives. Questions related to risk and perception of COVID-19 were added to the annual questionnaire and respiratory samples (currently anterior nasal swabs) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) molecular testing will be collected for participants with acute COVID-like symptoms within the preceding 7 days. We are also implementing a participatory surveillance system for acute illness (AIS) to complement annual sero-surveillance activities in identifying incident and recent arbovirus and SARS-CoV-2 infections. An automated text messaging system will be used to contact household representatives and other participating adults

who consent to participate in this additional activity weekly to inquire if any COPA participants in the household experienced fever or other COVID-like symptoms in the last 7 days. Project staff will contact households in which one or more participants reported symptoms to schedule an appointment to collect samples for arbovirus and SARS-CoV-2 molecular testing. Participants with a positive SARS-CoV-2 molecular test will be contacted by phone 2 to 4 weeks later for a follow-up questionnaire on symptoms, health care seeking, potential exposures, and outcomes of SARS-CoV-2 infection. We will use this data to inform public health recommendations and interventions to control SARS-CoV-2 transmission, including COVID-19 vaccine initiatives.

We have also added questions to the annual household representative questionnaire about frequency and type chemical insecticide use at the household level. This data will be used to inform entomological studies of *Aedes aegypti* mosquito insecticide resistance and recommendations for mosquito control in the Ponce region.

Finally, we have added questions to the annual individual and mobility and KAP questionnaires around dengue vaccine intention and uptake. The CDC's Advisory Committee on Immunization Practices (ACIP) voted on June 24th to advise that CDC recommend use of the first dengue vaccine approved by the FDA, Dengvaxia, in children aged 9 to 16 who have laboratory confirmation of prior dengue infection and live-in areas where dengue is endemic. Puerto Rico is a key target population for Dengvaxia and future dengue vaccines, and we will use data collected in COPA participants to inform development and roll-out of dengue vaccines on the island.

Burden and cost changes

In this Reinstatement, we provide updated estimates for the number of respondents based on participation rates in the most recent year. We also request OMB approval for changes to the content of all four questionnaires and for the addition of the AIS text messaging system, the AIS questionnaire, and the COVID-19 case follow up questionnaire. We present revised estimated burden per response for the four questionnaires and a new burden estimate for the AIS and COVID-19 case follow-up components. The forms were pretested to determine the revised estimates for burden per response. New questions relate primarily to COVID-19 and vaccine intention more broadly.

Estimates of annualized burden hours for this revision request will increase the total burden by 838 hours per year.

Taking into consideration that our sample size was reduced by 200 participants (from 4,000 to 3,800), some of the burden the questionnaires stayed the same or had only a slight increase in burden although questions were added.

Considering the added (attachment 3 - highlighted in green) and dropped questions (attachment 8 - highlighted in yellow) and after piloting the Household representative questionnaire, the average burden per response stayed the same relative to our last approval.

Considering the added (attachment 3 - highlighted in green) and dropped questions (attachment 8 - highlighted in yellow) and after piloting the Individual, Mobility, and Specimen Collection

questionnaires, the average burden per response increased by 5 minutes compared to our last approval.

Considering the added (attachment 3 - highlighted in green) and dropped questions (attachment 8 - highlighted in yellow) and after piloting the KAP questionnaire, the average burden per response stayed the same compared to our last approval.

Considering the added (attachment 3 - highlighted in green) and dropped questions (attachment 8 - highlighted in yellow) and after piloting the Vector Control questionnaire, the average burden per response decreased by 5 minutes compared to our last approval.

Because AIS is a new component for this project, the following questionnaires will add to the average total burden. The AIS text message will add 433 hours to the total burden, the AIS questionnaire will add 51 hours to the total burden, and the COVID-19 Case Follow-Up questionnaire will add 8 hours to the total burden. Because not all the cohort participants will participate in these components, the total addition to the burden is low.

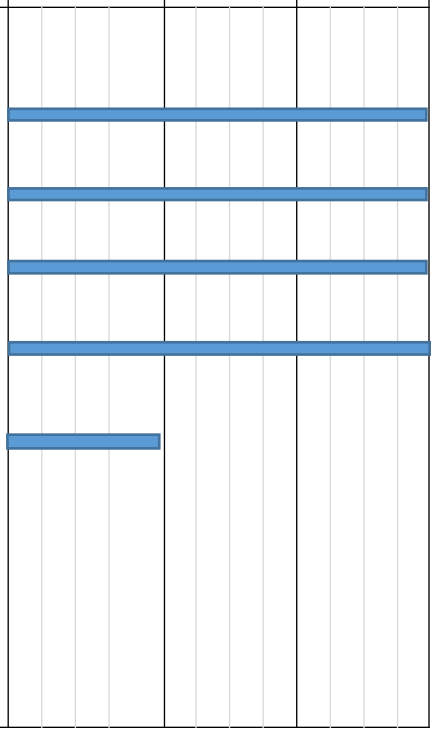
Estimates of annualized burden costs for this revision request will increase by $10,804 per year.

This increase is primarily due to the Puerto Rico minimum wage increase from $7.25 to $8.50 taking place on January 2022 and the addition of the AIS components.

16. Plans for Tabulation and Publication and Project Time Schedule

Progress reports are generated weekly, monthly, and annually to help monitor recruitment and data quality. After the first year of data collection, prevalence rates (as indicated by a positive IgG result to dengue, Zika or chikungunya viruses) will be calculated for each community. With the resulting data, for a future vector control intervention evaluation, clusters could be paired based on prevalence rates; among each pair, with intervention and control status randomly assigned. Annually, the incidence rate in each cluster will be assessed through arboviral disease testing After completion of the baseline in year 2, we will report on risk factors associated with arbovirus incidence and prevalence, attitudes towards traditional and novel vector control strategies, community attitudes and practices with regards to personal protection methods. Prevalence rates (as indicated by a positive IgG result to dengue, Zika or chikungunya viruses) will be calculated for each cluster. With the resulting data, for a future vector control intervention evaluation, clusters will be paired based on prevalence rates and movement frequency; among each pair, with intervention and control status will be randomly assigned. Annually, the incidence rate in each cluster will be assessed through arboviral disease testing. At the end of the 3-year follow up after implementation of the intervention, comparisons will be made between the intervention and control clusters using paired t-tests to assess any difference between groups.

Estimated dates for ongoing key activities are demonstrated in the table below.

MILESTONE	FY2022	FY2023	FY2024
• Lab testing human and vector[†§] • Industry partnership[*§] • Cohort follow up[*†] • Continuous AFI surveillance[*†] • Evaluation of intervention impact[*†§]			

*Will be supported by PHSU
† Will be supported by CDC
§ Will be supported by PRVCU

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

The OMB Expiration Date will be displayed.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

Attachments

1. Authorizing Legislation
2. Consent Forms
3. COPA questionnaire revision request
4. 60-day FRN
5. Privacy Impact Assessment
6. Consent summary
7. IRB Approval Letter
8. COPA questionnaire dropped questions
9. 30-day FRN