Request for Proposals (RFP)
Non-Targeted Testing of Chemicals in Drinking Water in California

California Breast Cancer Research Program
California Breast Cancer Prevention Initiatives

Deadline to apply
January 17, 2019

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Published November 8, 2018

About the California Breast Cancer Research Program and the California Breast Cancer Prevention Initiatives

The **California Breast Cancer Research Program (CBCRP)** was established pursuant to passage by the California Legislature of the 1993 Breast Cancer Act (i.e., *AB 2055 (B. Friedman) [Chapter 661, Statutes of 1993]* and *AB 478 (B. Friedman) [AB 478, Statutes of 1993]*). The program is responsible for administering funding for breast cancer research in the State of California.

The mission of CBCRP is to eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities.

- CBCRP is the largest state-funded breast cancer research effort in the nation and is administered by the University of California, Office of the President.
- CBCRP is funded through the tobacco tax, voluntary tax check-off on personal income tax forms, and individual contributions.
- The tax check-off, included on the personal income tax form since 1993, has drawn over $8.5 million for breast cancer research.
- Ninety-five percent of our revenue goes directly to funding research and education efforts
- CBCRP supports innovative breast cancer research and new approaches that other agencies may be reluctant to support.
- Since 1994, CBCRP has awarded over $280 million in 1,028 grants to 139 institutions across the state. With continued investment, CBCRP will work to find better ways to prevent, treat and cure breast cancer.

CBCPI Priority Areas

In 2004, CBCRP launched its Special Research Initiatives. The CBCRP's Breast Cancer Research Council devoted 30 percent of CBCRP research funds to support coordinated, directed, and collaborative research strategies that increase knowledge about and create solutions to both the environmental causes of breast cancer and the unequal burden of the disease.

In March 2010, CBCRP's Council decided to build on the existing SRI by devoting 50 percent of CBCRP research funds between 2011 and 2015. This new effort is titled the California Breast Cancer Prevention Initiatives (CBCPI). Approximately $24 million is being dedicated to directed, coordinated, and collaborative research to pursue the most compelling and promising approaches to:

1. Identify and eliminate environmental causes of breast cancer.
2. Identify and eliminate disparities/inequities in the burden of breast cancer in California.

3. Population level interventions (including policy research) on known or suspected breast cancer risk factors and protective measures.
4. Targeted interventions for high-risk individuals, including new methods for identifying or assessing risk.

To focus these research efforts, CBCRP issued a Request for Qualifications (RFQ) to fund a team to collaborate with CBCRP to develop and implement the California Breast Cancer Prevention Initiatives planning process. In 2010, the grant was awarded to Tracey Woodruff, PhD, MPH, Professor and Director of the University of California, San Francisco, Program on Reproductive Health and the Environment (PRHE).

In March 2015, CBCRP's Council approved fifteen (15) concept proposals to stimulate compelling and innovative research in all four topical areas of the CBCPI (environmental causes, health disparities, population-level interventions and targeted interventions for high risk individuals). A series of funding opportunities has been released reflecting these concepts.

Non-Targeted Testing of Chemicals in Drinking Water in California

Available Funding

This initiative aims to identify the presence of unknown and unregulated chemical mixtures in drinking water that can lead to breast cancer.

CBCRP intends to fund one project, with a maximum direct cost budget of $600,000 and a maximum duration of 5 years.

Completed responses to this RFP are due by the deadline: January 17, 2019. Signed face pages of submitted applications must be emailed to RGPOgrants@ucop.edu by **January 24, 2019**. The project start date is June 1, 2019.

For more information and technical assistance, please contact:
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Background/Justification

At least 10 percent of the nation's water systems are out of compliance with the Environmental Protection Agency's standards for drinking water quality (Environmental Protection Agency 2017). California is required to adhere to these standards and at times, the California State Water Resource Control Board actually creates more stringent maximum contaminant levels (MCLs) for chemicals found in drinking water. Public water systems in California are required to

meet primary drinking water standards which includes monitoring and reporting requirements for 33 synthetic organic contaminants, 28 volatile organic contaminants, 18 inorganic contaminants and 6 radionuclide contaminants (including alpha radiation) (California Department of Public Health, 2016).

Drinking water sources across California vary but two water sources—groundwater and the Sacramento/San Joaquin Rivers and Delta—provide over half of California's water supply (California Water Board 2012). Groundwater supplies 40% of California's water, and approximately 31 million Californians receive their drinking water from water systems that rely on groundwater (California Water Board 2013). Groundwater quality may be affected by a variety of natural and man-made contaminants. For example, the prominence of agriculture in California makes pesticides of particular concern, since they can find their way into groundwater, thus having the potential to affect aquatic and human health.

There are four state agencies (State Water Resources Control Board, California Department of Public Health, California Department of Food and Agriculture and Department of Water Resources) responsible for ensuring Californians have access to safe drinking water. Created in 1967, California's State Water Resources Control Board oversees surface and groundwater resources to ensure the highest water quality, with nine regional water quality control boards covering every county in California. The State Water Board monitors the quality of California's groundwater through the GAMA (Groundwater Ambient Monitoring and Assessment) Program. Created in response to the Groundwater Quality Monitoring Act of 2001, the GAMA Program provides groundwater information on key identified contaminants or constituents of concern (COCs) such as Tetrachloroehythene (PCE) and nitrates. The monitoring of COCs includes the detection levels of the COC in question (e.g. MCL levels), health effects of the COC and current methods used to treat the water for this contaminant.

The diversity and complexity of California water sources and filtration services also varies regionally. For example, Southern California imports almost all of its water from the Colorado River and the Sacramento-San Joaquin River Basin. San Diego County alone has four different water filtration centers. Two sources, four different filtration centers and seasonal variation in the chemical mixtures suggest variance in contaminants entering filtration but also different concentrations leaving these centers and into the public's drinking water. Regional differences exist also in concentration of pharmaceutical compounds with their concentration occurring most frequently in the Los Angeles area compared to the rest of the state (Fram et al 2011).

Research also suggests social disparities exist in drinking water quality. For example, uranium, which may be an endocrine-disrupting chemical, can be found in source water near mining and milling industries and exposures to uranium-laced drinking water may lead to reproductive health problems and cancer (Raymond-Whish et al 2007). Native tribes, particularly the Navajo, often have reservations near these industries suggesting unequal exposure to potentially harmful drinking water. Unequal exposures to potentially harmful chemicals in drinking water are not limited to Native American reservations. Drinking water in communities in California's San Joaquin Valley, for example, with higher proportions of racial/ethnic or lower income residents contain higher concentrations of nitrates, a key ingredient in fertilizers, even after having gone through water filtration (Balazs et al 2011).

Many of the emerging contaminants found in drinking water are largely overlooked in water-quality regulations, research and in their potential threat to human health (Bletsou et. al., 2015) and yet are found around the world (Westerhoff et al, 2005). Although there is substantial research on many common regulated environmental contaminants found in drinking water, little research has been devoted to characterizing its overall chemical mixture. Often regulation is limited to the parent chemical and little attention is given to the transformation products that result from chlorination, oxidation, methylation or some other process to treat or clean the water for consumption (Bletsou et al 2015). In fact, transformation products (TPs) are usually overlooked with very little knowledge about their toxicity and persistence (Aguera et al 2013). Water monitoring programs have historically focused on metals and only recently have shifted efforts to micro-pollutants, pharmaceuticals, personal care products and other potentially hormonally active chemicals and transformation products (Aguera et al 2013; Bletsou et al 2015; Ruff et. al., 2015).

Research identifying chemical mixtures and unknown chemical compounds in drinking water has been recommended as potential paradigm-shifting in both regulatory policy and drinking water quality. Additional research focused specifically on exposures to mammary gland carcinogens, mammary gland toxicants and endocrine disrupting chemicals that may be present in drinking water but not currently being regulated is also needed.

Thirty-two of the 216 mammary gland carcinogens identified by Rudel et al (1998) are commonly found in U.S. drinking water and less than half are regulated by the Safe Drinking Water Act. Very little is known about the nature and extent of toxic chemicals and their breakdown products found in drinking water and how they may influence breast cancer risk. One of the only studies to assess chemicals (specifically Tetrachloroethylene or PCE) in drinking water and breast cancer risk was a case-control study in Cape Cod, Massachusetts (Aschengrau et al 2003; Brody et al, 2006; Gallagher et al 2011). As methods and technology to assess exposure risk has improved, the latest analyses did show a modest increased risk for breast cancer for women with high exposure to PCE in their drinking water (Gallagher et al, 2011). What is needed (and are now available) are approaches that create precise information on breast cancer carcinogens, emerging contaminants with similar properties and their transformation products found in drinking water.

Historically, methods to determine the presence of particular environmental contaminants in water were limited by only those chemicals known and identified prior to sampling, yielding an analysis of only a small number of chemicals. However, this is now changing as mass spectrometry has become increasingly selective, sensitive and specific in its ability to identify and quantify pollutants (Aguera et. al 2013). Chemicals thought to be breast cancer carcinogens along with micro-contaminants and transformation products (many containing estrogenic properties) may be identified through a combination of targeted and non-targeted analyses using high resolution mass spectrometry. In fact, there is a newer method, “time-of-flight” technology (Ferrer et al 2003; Lacorte et al 2006), which can test water for every potential chemical that might be present. It is especially intended to detect unexpected or unknown compounds and has already been used to identify unknown chemicals in sewage effluent and human biological samples making the application of this method to drinking water now feasible (Hird et al 2014; Ruff et al 2015). Non-targeted analyses can be especially important because

although the chlorination of drinking water may eliminate the estrogenic activity for chemical components; it is unclear if the same is true for the transformation products created by chlorination (Bourgin et al 2013).

Regulation and the study of drinking water quality have so far mainly focused on known volatile and other serious contaminants known to have deleterious effects on human health. Currently, there may be breast cancer causing contaminants in our drinking water. With technology now available to uncover potentially harmful chemical mixtures in our drinking water, CBCRP seeks to support research to screen drinking water in California for unmonitored and unregulated chemicals and transformation products that are known and suspected mammary gland carcinogens, mammary gland toxicants and/or endocrine disrupting chemicals.

The results and methods developed from this research can stimulate future studies in population-level exposure of breast cancer causing carcinogens found in drinking water including focusing on specific geographic regions of concern and/or changes over time in type and concentration of these carcinogens. Conclusive findings can also be used to reduce toxic chemicals exposure and enact regulatory changes to better protect public health and reduce the risk of breast cancer.

Research Aims

The aims of this initiative are to:

1. Characterize the presence of chemicals in drinking water delivered from public water systems in a cross-section of California households. For the purpose of this research, chemicals include but are not limited to: industrial chemicals, agricultural chemicals, consumer product ingredients, and pharmaceuticals; unmonitored and unregulated commercial chemicals, The chemicals of particular interest for this initiative are those that are known and suspected mammary gland carcinogens, mammary gland toxicants, and/or endocrine disrupting chemicals.
2. Fill in the gaps of knowledge and focus on how drinking water quality may differ by region, water filtration center, etc. and how these differences may be mediated by social factors including community-level income levels, home ownership and other social factors.
3. Quantify the levels of the 10-15 most commonly detected mammary gland carcinogens, mammary gland toxicants and/or endocrine disrupting chemicals which have previously been unmeasured or underreported in drinking water.
4. Identify new chemical compounds, emerging contaminants or transformation products with notable concentrations in drinking water that could function as breast carcinogens.

Guidelines

Applicants should adhere to the following guidelines in developing their proposed research in response to this RFP. The proposed research should:

- Be conducted by a transdisciplinary collaborative team with demonstrated capacity to design and conduct each component of the study, including but not limited to expertise in analytic chemistry, environmental toxicology, exposure sciences, water sample access and collection capacity, and community engagement.
- Include community engagement in all aspects of the project.
- Indicate how the selection of the cross-sectional samples of drinking water supports the hypotheses/aims of the proposed research; takes into account and represents, as much as feasible, the diversity of California's water sources, seasonal variation and differences across filtration centers. Be sure to justify a water sampling strategy to best address the aims of the initiatives. CBCRP has a particular interest in gaps of knowledge about factors that may influence breast cancer hot spots, where the breast cancer incidence is higher than in surrounding communities and areas. CBCRP will also consider study designs that include bottled drinking water as one of the water samples.
- Describe how new chemicals, contaminants, emerging compounds and transformation products in drinking water will be identified. These new compounds may act as mammary gland carcinogens and can be the focus for further study, monitoring and regulation.
- Incorporate a study design that considers utilizing targeted, systematic and non-targeted analyses. Non-targeted analyses are required.
- Include a workflow for non-targeted analyses that should posit and support, with the literature, appropriate prioritization strategies/tools and data processing methods. Different approaches to tackling the amounts of data gained from non-targeted analyses pose both challenges but opportunities to further refine emerging strategies for environmental analyses of this type.
- Have a database, similar in structure and content to the GAMA program's database, characterizing the nature and extent of the mixture of chemicals in California's drinking water including their connection to breast cancer risk as one of the research deliverables.

A Note about Advocacy Involvement in Research

Advocacy involvement is a requirement for the research funded under this initiative. Therefore, applicants should select a breast cancer or other appropriate community advocate(s), affiliated with an organization, to be actively involved in the proposed research. Applications will be evaluated on the extent to which advocates are substantively involved in the project including identification of an appropriate advocate(s) for the proposed research; a detailed description of how the advocate(s) will be involved in the project; submission of a Letter of Commitment co-signed by the research advocate(s) and the PI; and a budget line item and justification covering the advocate(s) time, effort, and expenses on the project (e.g. at least quarterly, in-person meetings with the advocate and the investigative team). If needed, CBCRP staff can assist investigators with meeting the advocacy involvement requirement as they prepare their applications.

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How We Evaluate RFPs

CBCRP uses a two-tier evaluation process: peer review and programmatic review. It is a combination of (i) the peer review rating, (ii) the programmatic rating, and (iii) available funding that determines a decision to recommend funding.

Peer Review
All applications are evaluated by a peer-review committee of individuals from outside of California. The committee is comprised of scientists from relevant disciplines and breast cancer advocates and other community representatives.

- **Innovation** Extent to which the project explores new and potentially useful information to identify chemical mixtures in California drinking water. Are the concepts and hypotheses speculative and exploratory? Are methods novel and original? Has(ve) the investigator(s) thought creatively about how to sample and measure the chemical mixtures in drinking water as well as their relationship to breast cancer?

- **Impact:** Potential for the project, if successful, to change policy for or regulation of drinking water chemical content and additives. Does the research have the ability to translate to population-level change? Will the data yielded by the research be to sufficient to inform policy or future research directions?

- **Approach:** The quality, organization, and presentation of the research plan, including methods and analysis plan. Will the research planned answer the research questions? Are the design, methods and analyses well-developed, integrated and appropriate to the aims and stated milestones of the project? Does the application demonstrate an understanding of the research question and aims?

- **Feasibility:** The extent to which the aims are realistic for the scope and duration of the project; adequacy of investigator's expertise and experience, and institutional resources; and availability of additional expertise and integration of multiple disciplines. Does the investigator (and do co-investigators) have demonstrated expertise and experience working in the topic area? Can the project be completed as proposed given the available funding, time frame and the staff knowledge, skills, experience, and institutional resources?

Programmatic Review
This review is conducted by the Breast Cancer Research Council and involves reviewing and scoring applications with sufficient scores from the peer review process based on the criteria listed below. The individuals on the Council performing this review include advocates, clinicians, and scientists from a variety of disciplines. In performing the Programmatic Review the advisory

Council evaluates **only a portion of the application materials** (exact forms are underlined). Pay careful attention to the instructions for each form. The Programmatic criteria include:

- **Responsiveness.** How responsive are the project and PI to the stated intent of the selected Initiative? Compare the PI's statements on the Other Review Criteria form and the content of the Lay and Scientific Abstracts to the CBCPI topic area. (A score of "0" for Responsiveness is an automatic disqualification.)

- **Dissemination and translation potential.** The degree to which the applicant's statements on the Other Review Criteria form provides a convincing argument that the proposed research has the potential to inform the development and/or implementation of California chemicals policy and regulation.

- **Quality of the lay abstract.** Does the Lay Abstract clearly explain in non-technical terms the research background, questions, hypotheses, and goals of the project? Is the relevance to the research initiative understandable?

- **Addressing the Needs of the Underserved.** Do the project and the PI's statements on the Other Criteria template demonstrate how this research will address the needs of the underserved (including those that are underserved due to factors related to race, ethnicity, socioeconomic status, geographic location, sexual orientation, physical or cognitive abilities, age, occupation and/or other factors)?

- **Advocacy Involvement.** Are the named advocate(s) and advocacy organization appropriate for the proposed research project? Were they engaged in the application development process? Are meetings and other communications sufficient for substantive engagement? Are the roles and responsibilities of the PI and the advocate(s) clearly outlined and is the agreement for advocate compensation and reimbursement clear? [The Advisory Council will examine the PI's statements on the Lay and Scientific Abstracts and Advocacy Involvment forms.]

Application Process and Instructions

Submission Deadline: Applications must be submitted through proposalCENTRAL (https://proposalcentral.altum.com/) by Thursday, January 17, 2019 at 12 NOON Pacific Standard Time.

Signed face pages of submitted applications must be emailed to RGPOgrants@ucop.edu by 5pm January 24, 2019.

proposalCENTRAL Online Submission Instructions

Formatting Instructions

All submissions must be in **English**.

Follow these format requirements for written text (consistent with NIH/PHS 398 form):

- The height of the letters must not be smaller than 11 point. Times New Roman or Arial are the suggested fonts.
- Type density must be no more than 15 characters per inch (cpi).
- Page margins, in all directions, must be at least 1/2 inch.
- PI(s) last names and first initials must be in a header, on each page, flush right.

Deviations from the page format, font size, specifications and page limitations are grounds for CBCRP to reject and return the submission without peer review.

Online Application (Proposal) Management

CBCRP requires applications be submitted via an online system: proposalCENTRAL. Following are instructions on how to register and how to submit your response to the RFP. The submission deadline is 12 noon Pacific Time, January 17, 2019. *Note*: the proposalCENTRAL site shows East Coast times. Do NOT wait until the deadline to submit your application; if you miss the deadline, the system will not allow you to submit.

If you have any problems using proposalCENTRAL, please contact the proposalCENTRAL help line at (800) 875-2562.

Online Registration

The PIs as well as the institution's signing official, contracts & grants manager and fiscal contact must be registered in proposalCENTRAL: https://proposalcentral.altum.com/. Start with "Click here to register". Fill out all the necessary fields on the registration page: First Name, Last Name, Email Address, User ID (can be your name), Password (case-sensitive), Challenge Question, and Answer.

Click BOTH BOXES on the bottom of the page to confirm your agreement with their "Terms of Service" and "Acceptable Use Policy." Click on the "Register" button. ProposalCENTRAL will send you an email with your username, password and a confirmation number. Once confirmed, you can login and the first time you enter the system, it will ask you to enter the confirmation number. You won't need that number again.

Online Forms and Fields

Once logged on, select the "Grant Opportunities" (gray) tab on the top of the page. Open up the filter and scroll down to California Breast Cancer Research Program. Sort the available funding by CBCRP and all of the funding opportunities for CBCRP will be showing. Choose the Drinking Water Initiative and click on "Apply Now" at the far right of the line.

Portions of the application are prepared using pre-formatted web pages in proposalCENTRAL (Proposal Sections 1 and 3-8). To move from section to section you can click the "Next" button to both save your work and go to the next section, or click "Save" and then click on the next section.

Proposal Section 2 allows you to download the Templates and Instructions for the CBCRP forms. After completing the forms on your computer, Proposal Section 9 allows you upload each one as PDF to attach it to your application.

❒ Section 1: Title Page

The individual being designated as the Applicant/PI should log onto proposalCENTRAL first to begin the submission process.

On the "Title Page" enter the Project Title in the space provided (do not exceed 60 characters). Enter the total budget amount requested for the project, including indirect costs, if eligible. The projected start date for this project is June 1, 2019. Enter the end date of the project (up to 60 mos).

❒ Section 2: Download Templates & Instructions

This section includes these instructions as well as the relevant application forms. You will need these forms in order to respond to this RFP.

❒ Section 3: Enable Other Users to Access this Proposal

Note: A person must be registered in proposalCentral before s/he can be given access.

Click on "Enable Other Users to Access this Proposal" (the left side in the gray box). Read this page thoroughly to understand the different levels of access you can grant others to your application.

At the bottom of that page, in "Proposal Access User Selection," type in the email address of other individuals who will be working on the application (they should all have completed the registration process prior to being enabled) and then click "Find User."

Select "View," "Edit," or "Administrator" for the level of access they will have.

Click "Accept Changes" to save this page.

❒ Section 4: Applicant/PI

Click on "Applicant/PI" and make sure that all required fields (identified with a red asterisk) are complete. Click "Edit Professional Profile" to enter any missing data. **A required field entitled "ORCID ID" has been added to Professional Profile Page, at the bottom of Section 4: Personal Data for Applications.** ORCID provides a persistent digital identifier that distinguishes you from every other researcher and, through integration in key research workflows such as manuscript and grant submission, supports automated linkages between you and your professional activities ensuring that your work is recognized. If you have not already obtained an ORCID ID number, you may do so here: http://orcid.org/. Once you have done so, please enter your 16-digit identifier in the space provided on your profile page in the following format: xxxx-xxxx-xxxx-xxxx.

Click "Return to Proposal" after entering missing data. Enter the % effort that the PI will devote to this project. The minimum effort is 10% FTE. Click "Save."

❒ Sections 5: Institution & Contacts

On the "Institution & Contacts" page, make sure that all required fields (identified with a red asterisk) are complete, including the Signing Official, Contracts and Grants Official, and Fiscal (Accounting) Contact for the applicant institution. To complete these fields select the name or enter the email address of the individual in each of those roles and click "Add."

If you add someone, the "Contact Screen - Applicant Institution" screen will open. Make sure that all required fields (identified with a red asterisk) are completed. Click "Save", then click "Close Window". Then click "Save" on the Institution & Contacts page.

❒ Section 6: CSO Codes and Keywords

On this page you should select and add CSO codes. There are seven major CSO categories, and each of these is divided into 4-9 sub-categories. The CSO coding scheme is presented in the Web site https://www.icrpartnership.org/cso in the downloads section in the upper right hand corner. Choose a major heading for your research and read the subcategory description. Choose the one that most closely fits. If your project fits under more than one CSO category, add a second code. The second code should represent a different, but integral, part of the research and about half of the total effort.

In addition, add three key words (1-3 words) that describe your project's main topic, technology, or methods. This helps to place it in the appropriate review committee and assign reviewers. Please use words not in the title.

❒ Section 7: Budget

Provide the total costs for the entire funding request for the grant year on this page. Make sure the budget numbers are exactly the same as those in the provided Excel Budget Summary form that you upload.

❒ Section 8: Organization Assurances

Provide any required information for Human Subjects. If assurances will be required and have not yet been received, mark "pending" and enter the (proposed) date of submission in the "Approved or Pending Date".

❒ Section 9: Upload RESEARCH PLAN and Other Attachments

This page contains a duplicate list of the forms and instructions that are in Download Templates and Instructions (above and Proposal Section 2). This is where you will upload the CBCRP forms and any other attachments to your proposal; the required items are listed.

To upload attachments, fill in the fields at the top of the page:

- **Describe Attachment:** Provide a meaningful description, such as Jones CV.
- **Select Attachment Type:** From the drop down menu, select the type of form that is being attached.
- **Allowable File Type:** Only an Adobe PDF document may be uploaded. Do not password protect your documents. Help on converting files to PDF can be found on the proposalCentral site at https://proposalcentral.altum.com/FAQ/FrequentlyAskedQuestions.asp.
- **Select File From Your Computer to attach:** The Browse button allows you to search for the PDF on your computer; click Open to select the file.

Note: Explicit instructions on the content of the documents to be uploaded follow in the "Instructions for CBCRP Forms" section.

❒ Section 10: PI ORCID ID

This section is a reminder to returning investigators to obtain and enter an ORCID ID number by editing your professional profile using the link that appears here. At the bottom of Section 4 in your profile (Personal Data for Applications), you will find the space to enter your 16 digit ORCID ID number and a link to obtain one if necessary. Please enter the information in the following format: xxxx-xxxx-xxxx-xxxx.

❒ Section 11: Validate

This function allows you to check whether all required items have been completed and attached. Don't wait until the last minute to check! Validate often during the course of completing your application so you have time to address missing items. Clicking the "Validate" button will either result in a link to missing items so you can easily go to the page and complete them, or a message at the top of the page "Has been validated and is ready to submit."

❒ Section 12: Print Face Page When Application Complete

Applicants must print application's Face Page and obtain the necessary PIs and institutional signing official signatures within a week of the electronic submission (see below).

❒ **Section 13: Submit**

Submission is only possible when all required items have been completed and all required forms have been attached. Once an applicant hits "Submit," the application cannot be recalled.

❒ **Outside of proposalCENTRAL: Email Face Page Submission**

The PIs, institution's signing official, Contract and Grants official and Fiscal (or Accounting) official all must sign the printed Face Page. Scan the signed form as a PDF and email to RGPOGrants@ucop.edu before 5 pm (Pacific Time) by January 24, 2019.

CBCRP Uploaded Form Instructions

Lay Abstract (REQUIRED)

This item is evaluated mainly in the programmatic review. The Lay Abstract is limited to one page and must include the following sections:

- A non-technical introduction to the research topics
- The question(s) or central hypotheses of the research in lay terms
- The general methodology in lay terms
- Innovative elements of the project in lay terms

The abstract should be written using a style and language comprehensible to the general public. Avoid the use of acronyms and technical terms. The scientific level should be comparable to either a local newspaper or magazine article. Avoid the use of technical terms and jargon not a part of general usage. Place much less emphasis on the technical aspects of the background, approach, and methodology. Ask you advocate partner to read this abstract and provide feedback.

Scientific Abstract (REQUIRED)

This item is evaluated mainly in the peer review. The Scientific Abstract is limited to one page and should include:

- A short introductory paragraph indicating the background and overall topic(s) addressed by the research project
- The central hypothesis or questions to be addressed in the project.
- A listing of the objectives or specific aims in the research plan
- The major research methods and approaches used to address the specific aims
- A brief statement of the impact that the project will have on breast cancer.

Provide the critical information that will integrate the research topic, its relevance to breast cancer, the specific aims, the methodology, and the direction of the research in a manner that will allow a scientist to extract the maximum level of information. Make the abstract understandable without a need to reference the detailed research plan.

Other Review Criteria (REQUIRED)

This item is evaluated in the programmatic review. Limit the text to two pages. The CBCRP Council (who conducts the programmatic review) will NOT see your Research Plan. The information on this template allows the CBCRP Research Council to rate the application for adherence to the objectives of the CBCPI research area as outlined in the specific RFP.

CBCPI Focus (Responsiveness): Provide a clear, brief summary for the CBCRP Council (1 or 2 paragraphs) of how your proposed research addresses the specific RFP topic area, by increasing or building on specific scientific knowledge; by pointing to additional solutions to identify and eliminate environmental causes, and or disparities in, breast cancer; and/or, by helping identify or translate into potential prevention strategies.

Addressing the Needs of the Underserved. Describe how this research will address the needs of the underserved (including those that are underserved due to factors related to race, ethnicity, socioeconomic status, geographic location, sexual orientation, physical or cognitive abilities, age, occupation and/or other factors)?

Dissemination and Translation Potential: Describe how research findings will be shared with various stakeholder audiences (i.e., policymakers, community members, breast cancer advocates, other researchers/agencies, health care providers, funders etc.). Describe the potential for how the research findings will be translated into policy and/or other practice.

Advocacy Involvement (REQUIRED)

Follow the instructions on the form, and be sure to address the requested three items (Advocacy Organization/Advocate(s) Selection and Engagement to Date, Advocate(s) Role in Proposed Research and Meeting and Payment Plans). Limit the text to one page.

Discuss what involvement, if any, advocates had in the development of this proposal and will have in the project, if funded. Explain how this proposal shows awareness and inclusion of breast cancer advocacy concerns involved in the proposed research.

Letter(s) of Commitment (REQUIRED)

Please use the template as a basis for commitment letters from the advocate, scientific and/or subcontracting individuals/institutions. Limit the text to two pages.

Budget Summary (REQUIRED)

Please enter the budget for the presented categories by year into the summary sheet (Excel format). Additional instructions are presented on the form.

The maximum duration and direct costs may not exceed the following for the RFP *Non-Targeted Testing of Chemicals in Drinking Water in California.*

Research Study (1 project):	5 years & $600,000

Note: The amount of the subcontracted partner's F&A costs can be added to the direct costs cap. Thus, the direct costs portion of the grant to the recipient institution may exceed the award cap by the amount of the F&A costs to the subcontracted partner's institution.

Personnel. List the PI for the application and "individuals who contribute in a substantive way to the scientific development or execution of the project, whether or not salaries are requested." (NIH definition). Include those at the level of postdoctoral fellow and higher. Upload a NIH "Biographical Sketch and Other Support" form for each individual listed. The minimum "Months Devoted to Project" required for the PI is 1.2 months (= 10% FTE).

Other Project Expenses. Enter the costs associated with each category presented on the template (description to be provided in Budget Justification).

Advocate(s) Expenses. Include any travel, meeting, and consultation costs/fees associated with advocate engagement.

Equipment. Purchases up to $10,000 are allowed. Only include individual items >$5,000. Any items less than $5,000 must be purchased under the "supplies" budget category above.

Travel Expenses. Requested travel costs must be broken down and justified as Project-related, Annual meeting (third year only) or Scientific meeting (PI only capped at $2,000 per year).

Subcontracts. In the case of University of California applicants, subcontracts need to be categorized and broken out as one of two types, University of California-to-University of California (UC to UC) sub agreements or transfers; or, Other. Both categories require additional description (Budget Justification) and documentation (Appendix).

Service Agreements and Consultants. Both categories require additional description (Budget Justification) and documentation (Appendix).

Pooled Expenses. The RGPO takes a conservative budgeting approach to the allocation of pooled expenses. Pooled expenses such as insurance surcharges, system wide networking surcharges, and other pooled training and facilities expenses are generally disallowed as direct costs. Pooled expenses may be allowed at the discretion of the RGPO Program Director if the grantee can show that: 1) the project to be funded will be directly supported by the pooled expenses, 2) the pooled expenses have been

specifically excluded from the indirect cost rate negotiation, and 3) the pooled expenses have been allocated consistently over time within the organization (e.g. it is not allowable to charge a new indirect expense such as "facilities" as a direct line item in order to recoup funds lost due a poorly negotiated rate agreement). No indirect cost recovery will be allowed on pooled expenses.

Indirect (F&A) costs. Non-UC institutions are entitled to full F&A of the Modified Total Direct Cost base (MTDC); UC institutional F&A is capped at 25% MTDC*

**Allowable expenditures in the MTDC base calculation include salaries, fringe benefits, materials and supplies, services, travel, and up to the first $25,000 of each subgrant or subcontract (regardless of the period covered by the subgrant or subcontract). Equipment, capital expenditures, charges for patient care and tuition remission, rental costs, scholarships, and fellowships as well as the portion of each subgrant and subcontract in excess of $25,000 shall be excluded from the modified total direct cost base calculation.*

Please see the RFP under **Allowable Indirect (F&A) Costs** for more information.

Budget Justification & Facilities (REQUIRED)

This item is evaluated in the peer review. Limit the text to two pages. Follow the instructions on the template. The minimum "Months Devoted to Project" required for each PI is 1.2 months (= 10% FTE).

Key Personnel (REQUIRED)

This item is evaluated in the peer review. Limit the text to one page. Follow the instructions on the template.

Biographical Sketch & Other Support (REQUIRED)

This item is evaluated in the peer review. Use the NIH form. Limit the length of each biosketch to *no more than* five (5) pages.

Research Plan (REQUIRED)

This section is the **most important** for the peer review. Note carefully the page limits, format requirements, and suggested format.

Page limit: 12 pages

An additional 3 pages is allowed for References.

Format issues: Begin this section of the application using the template. Subsequent pages of the Research Plan and References should include the principal investigator's name (last, first, middle initial) placed in the upper right corner of each continuation page.

The Research Plan and all continuation pages must conform to the following four format requirements:

1. The height of the letters must not be smaller than 11 point; Times New Roman or Arial are the suggested fonts.
2. Type density, including characters and spaces, must be no more than 15 characters per inch (cpi).
3. No more than 6 lines of type within a vertical inch;
4. Page margins, in all directions, must be at least ½ inch.

Use the appendix to supplement information in the Research Plan, not as a way to circumvent the page limit.

Suggested outline:

Introduction and Hypotheses: Provide a brief introduction to the topic of the research and the hypotheses/questions to be addressed by the specific aims and research plan. The relationship of the project to the specific CBCPI Project Type and expectations outlined within the RFP should be clear.

Specific Aims: List the specific aims, which are the steps or increments deemed necessary to address the central hypothesis of the research. The subsequent research plan will detail and provide the approach to achieving each of these aims.

Background and Significance: Make a case for your project in the context of the current body of relevant knowledge and the potential contribution of the research.

Preliminary Results: Describe the recent work relevant to the proposed project. Emphasize work by the PI and data specific to breast cancer, water and non-targeted mass spectrometry.

Research Design and Methods: Provide an overview of the experimental design, the methods to be used, and how data is to be collected and analyzed. Describe the exact tasks related to the Specific Aims above. Provide a description of the work to be conducted during the award period, exactly how it will be done, and by whom. Include a letter of commitment if the applicant PI will be using a data set that they do not control/own. Recognition of potential pitfalls and possible alternative approaches is recommended. How will technical problems be overcome or mitigated? Cover all the specific aims of the project in sufficient detail. Identify the portions of the project to be performed by any collaborators. Match the amount of work to be performed with the budget/duration requested. A timeline at the end will demonstrate how the aims are interrelated,

prioritized, and feasible. Explain the use of human subjects and vertebrate animals and show their relationship to the specific aims.

Resources and Facilities: Describe the resources and facilities to be used (e.g., laboratory space, core facilities, major equipment, access to populations, statistical resources, animal care, and clinical resources) and indicate their capacities, relative proximity and extent of availability. Include an explanation of any consortium/ contractual arrangements with other organizations regarding use of these resources or facilities. Describe resources supplied by subcontractors and those that are external to the institution. Make sure all of the research needs described in the research plan are addressed in this section.

Human Subjects (OPTIONAL)

This item is evaluated in the peer review. **This form is required only for applications that use Human Subjects, including those in the "Exempt" category. Use additional pages, if necessary. For applications requesting "Exemption"** from regular IRB review and approval please provide sufficient information in response to item #1 below to confirm there has been a determination that the designated exemptions are appropriate. **The final approval of exemption from DHHS regulations must be made by an approved Institutional Review Board (IRB).**

Documentation must be provided before an award is made. Research designated exempt is discussed in the NIH PHS application: https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.500-phs-human-subjects-and-clinical-trials-information.htm#1.2. The categories of research that qualify for exemption are defined in the Common Rule for the Protection of Human Subjects. These regulations can be found at 45 CFR 46. Many research projects funded by CBCRP fall into Exemption category #4. Even if a grant application is exempt from these regulations, it must, nevertheless, *indicate the parameters of the subject population* as requested on the form.

For applications needing full IRB approval: If you have answered **"YES"** on the Organization Assurances section of the CBCPI Application Face Page and designated no exemptions from the regulations, the following **seven points** must be addressed. In addition, when research involving human subjects will take place at collaborating site(s) or other performance site(s), provide this information before discussing the seven points. Although no specific page limitation applies to this section, be succinct.

1. Provide a detailed description of the proposed involvement of human subjects in the project.
2. Describe the characteristics of the subject population, including its anticipated number, age range, and health status. It is the policy of the State of California, the University of California, and CBCRP that research involving human subjects must include members of underserved groups in study populations. Applicants must describe how minorities will be included and define the criteria for inclusion or exclusion of any sub-population. If this requirement is not satisfied, the rationale must be clearly explained and justified.

Also explain the rationale for the involvement of special classes of subjects, if any, such as fetuses, pregnant women, children, prisoners, other institutionalized individuals, or others who are likely to be vulnerable. Applications without such documentation are ineligible for funding and will not be evaluated.

3. Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records or data.
4. Describe the plans for recruiting subjects and the consent procedures to be followed, including: the circumstances under which consent will be sought and obtained, who will seek it; the nature of the information to be provided to the prospective subjects; and the method of documenting consent.
5. Describe any potential risks —physical, psychological, social, legal, or other. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.
6. Describe the procedures for protecting against, or minimizing, any potential risks (including risks to confidentiality), and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects on the subjects. Also, where appropriate, describe the provision for monitoring the data collected to ensure the safety of subjects.
7. Discuss why the risks are reasonable in relation to the anticipated benefits to subjects, and in relation to the importance of knowledge that may be reasonably expected to result.

Documentation of Assurances for Human Subjects

In the appendix, if available at the time of submission, include official documentation of the approval by the IRB, showing the title of this application, the principal investigator's name, and the approval date. Do not include supporting protocols. Approvals obtained under a different title, investigator or organization are *not* acceptable, unless they cross-reference the proposed project. Even if there is no applicant institution (i.e., an individual PI is the responsible applicant) and there is no institutional performance site, an USPHS-approved IRB must provide the assurance. If review is pending, final assurance should be forwarded to CBCRP as soon as possible**.** Funds will not be released until all assurances are received by CBCRP. If the research organization(s) where the work with human subjects will take place is different than the applicant organization, then approvals from the boards of each will be required.

Data and Safety Monitoring Boards (DSMB)

Applications that include Phase I-III clinical trials may be required to provide a data and safety monitoring board (DSMB) as described in the NIH policy release, http://grants.nih.gov/grants/guide/notice-files/not98-084.html. This ensures patient safety, confidentiality, and guidelines for continuing or canceling a clinical trial based on data collected

in the course of the studies. CBCRP may require documentation that a DSMB is in place or planned prior to the onset of the trial.

Appendix List (OPTIONAL)

Follow the instructions and items list on the template. **The appendix may not be more than 30 pages in length.**

Note that the *research plan must be self-contained* and understandable without having to refer to the appendix. Only those materials necessary to facilitate the evaluation of the research plan or renewal report may be included.

General Funding Policies

Eligibility and Award Limits

1. Any individual or organization in California may submit an application. The research must be conducted primarily in California. We welcome investigators from community organizations, public or privately owned corporations and other businesses, volunteer health organizations, health maintenance organizations, hospitals, laboratories, research institutions, colleges, and universities.
2. We encourage researchers new to breast cancer to apply. Applicants who have limited experience in breast cancer research should collaborate with established breast cancer researchers.
3. PIs who have previously been funded by CBCRP are welcome to apply, but the research aims must be distinct from their previous CBCRP grants.
4. Multiple applications and grant limits for PIs. A PI may submit more than one application, but each must have unique specific aims. For Cycle 25 applicants are limited to a maximum of two (2) grants either as PI or co-PI, and these must be in different award types. The Research Initiative grants are not included in this limit. A PI may have more than one Research Initiative grant in a year.

Policy on Applications from PIs with Delinquent CBCRP Grant Reports

PIs with current CBCRP grant support will not be eligible to apply for additional funding unless the required scientific and fiscal reports on their existing grants are up-to-date. This means that Progress/Final Scientific Reports or Fiscal Reports that are more than one month overdue may subject a Cycle 25 application to possible disqualification unless the issue is either, (i) addressed by the PI and Institution within one month of notification, or (ii) the PI and Institution have received written permission from CBCRP to allow an extension of any report deadlines.

Application Revision Guidelines

A revised application must have the same principal investigator as the original application. When possible it should have the same title as the original application. However, if the specific aims of the project have changed sufficiently, then a modified title may be chosen. A revision submission for all eligible award types (except CRCs) must include a section of not more than 2 pages uploaded as a part of the Research Plan. This section is a summary of the substantial additions, deletions, and changes that have been made. It must also include responses to criticisms in the previous Review Committee evaluation. This material does not count towards the normal page limit for the Research Plan. We also recommend emphasizing in the Research Plan any relevant work done since the previous application. CRC applicants should follow the directions in the CRC application materials regarding resubmissions.

Confidentiality

CBCRP maintains confidentiality for all submitted applications with respect to the identity of applicants and applicant organizations, all contents of every application, and the outcome of

reviews. For those applications that are funded CBCRP makes public, (i) the title, principal investigator(s), the name of the organization, and award amount in a "Compendium of Awards" for each funding cycle, (ii) the costs (both direct and indirect) in CBCRP's annual report, (iii) the project abstract and progress report abstracts on the CBCRP Web site. If the Program receives a request for additional information on a funded grant, the principal investigator and institution will be notified prior to the Program's response to the request. Any sensitive or proprietary intellectual property in a grant will be edited and approved by the PI(s) and institution prior to release of the requested information.

No information will be released without prior approval from the PI for any application that is not funded.

Human Subjects and Vertebrate Animal Use

If a project proposes activities that pose unacceptable potential for human and animal subject risks, then a recommendation either not to fund or to delay funding until the issue is resolved may result.

IRB approval, human subject "exemption" approval, or animal assurance documentation must be provided prior to funding, but is not needed for application review. Applicants are encouraged to apply to the appropriate board or committee as soon as possible in order to expedite the start of the project, and you must do so before or within 21 days of notification that an award has been offered. If all reasonable efforts are not made to obtain appropriate approvals in a timely fashion, funds may be reallocated to other potential grantees' proposed research projects.

Award Decisions

Applicants will be notified of their funding status by April 1, 2019. The written application critique from the review committee, the merit score average, component scores, percentile ranking, and programmatic evaluation are provided at a later time. Some applications could be placed on a 'waiting list' for possible later funding.

Appeals of Funding Decisions

An appeal regarding the funding decision of a grant application may be made only on the basis of an alleged error in or deviation from, a stated procedure (e.g., undeclared reviewer conflict of interest or mishandling of an application). Details concerning the appeals procedure may be obtained from the appropriate Research Administrator (with whom the applicant is encouraged to discuss his/her concerns), the CBCRP Director, or by contacting us through the CBCRP Web site: www.cabreastcancer.org/. The period open for the appeal process is within 30 days of receipt of the application evaluation from the Program office. Contact CBCRP to obtain full information on the appeals process.

Final decisions on application funding appeals will be made by the UCOP Research Grant Program Office (RGPO) Interim Executive Director Julia Arno. Applicants who disagree with the

scientific review evaluation are invited to submit revised applications in a subsequent grant cycle with a detailed response to the review.

Pre-funding Requirements

Following notification by CBCRP of an offer of funding, the PI and applicant organization must accept and satisfy normal funding requirements in a timely manner. Common pre-funding items include:

- Verification of Principal Investigator status from an appropriate institutional official.
- Documentation of 501(c)(3) non-profit organization status for the organizations.
- Documentation of the DHHS-negotiated (or equivalent) indirect cost rate for non-U.C. institutions.
- Supply up-to-date documentation for approved indirect rate (F&A costs) agreements as of the grant's start date and any derived calculations, if applicable.
- Supply any missing application forms or materials, including detailed budgets and justifications for any subcontract(s).
- IRB applications or approvals pertaining to the award.
- Resolution of any scientific overlap issues with other grants or pending applications.
- Resolution of any Review Committee and Program recommendations, including specific aims, award budget, or duration.
- Modify the title and lay abstract, if requested.

Open Access Policy

As a recipient of a California Breast Cancer Research Program (CBCRP) grant award, you will be required to make all resulting research findings publicly available in accordance with the terms of the Open Access Policy of the Research Grants Program Office (RGPO) of the University of California, Office of the President (UCOP). This policy, which went into effect on April 22, 2014, is available below:

RGPO Open Access Policy

The UCOP Research Grants Program Office (RGPO) is committed to disseminating research as widely as possible to promote the public benefit. To that end, all RGPO grantee institutions and researchers grant RGPO a nonexclusive, irrevocable, worldwide license to exercise any and all rights under copyright and in any medium for all scholarly articles and similar works generated as a result of an RGPO grant award, and agree to authorize others to do the same, for the purpose of making their articles widely and freely available in an open access repository. This policy does not transfer copyright ownership, which remains with the author(s) or copyright owners.

Scope and Waiver (Opt-Out)

The policy applies to all scholarly articles and similar works authored or co-authored as a result of research sponsored by an RGPO grant, except for any articles published before the adoption of this policy and any articles for which the grantee institution and/or researchers entered into an incompatible licensing or assignment agreement before the adoption of this policy. Upon

express written request of the institutional grantee and/or researcher, RGPO will waive the license for a particular article or delay "open access" to the article for a specified period of time.

Deposit of Articles

To assist the RGPO in disseminating and archiving the articles, the grantee institution and all researchers to the grant award will commit to helping the RGPO to obtain copies of the articles that are published as a result of an RGPO sponsored grant award. Specifically, each author will provide an electronic copy of his or her final version of the article to the RGPO by the date of its publication for inclusion in an open access repository, subject to any applicable waiver or delay referenced above. Notwithstanding the above, this policy does not in any way prescribe or limit the venue of publication.

Grant Management Procedures and Policies

Details concerning the requirements for grant recipients are available in a separate publication, the University of California, Office of the President, "RGPO Grant Administration Manual." The latest version of the Manual and programmatic updates can be obtained from the Program's office or viewed on our Web site: http://www.ucop.edu/research-grants-program/grant-administration/index.html.