



Request for Proposals (RFP)
**Identify Novel Biological Markers of Breast Cancer Risk Related to Environmental
 Chemical Exposures**

California Breast Cancer Research Program
California Breast Cancer Prevention Initiatives

Deadline to apply
Friday, April 8, 2016

Table of Contents

About CBCRP & CBCPI	2
CBCPI Priority Areas	2
Identify Novel Biological Markers of Breast Cancer Risk Related to Environmental Exposures	4
Available Funding	4
Background/Justification	4
Research Aims	6
Project Guidelines and Example Research Topics	7
Budget	8
References	8
How We Evaluate RFPs	10
Application Process and Instructions	12
ProposalCENTRAL Submission Instructions	12
CBCRP Uploaded Forms Instructions	15
General Funding Policies	23
Eligibility and Award Limits	23
Policy on Applications from PIs with Delinquent CBCRP Grant Reports	23
Application Revision Guidelines	23
Confidentiality	23
Human Subjects and Vertebrate Animal Use	24
Award Decisions	24
Appeals of Funding Decisions	24
Pre-funding Requirements	24
Open Access Policy	25
Grants Management Procedures and Policies	26

California Breast Cancer Research Program & California Breast Cancer Preventions 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 the CBCRP is to eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities.

- The 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
- The 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
- The CBCRP supports innovative breast cancer research and new approaches that other agencies may be reluctant to support.
- Since 1994, CBCRP has awarded over \$262 million in 1,006 projects to over 100 academic institutions and community organizations across the state. With continued investment, the CBCRP will work to find better ways to prevent, treat and cure breast cancer.

CBCPI Priority Areas

In 2004, the 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. Approximately \$24 million will be 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, the CBCRP issued a Request for Qualifications to fund a team to collaborate with the 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 will be released over the next two years reflecting these concepts.

Identify Novel Biological Markers of Breast Cancer Risk Related to Environmental Chemical Exposures

Available Funding

This initiative aims to investigate upstream biomarkers of breast cancer risk and identify novel biomarkers of previous exposure to chemicals known or suspected to contribute breast cancer.

It is anticipated that funding will be available for this initiative to support up to three projects for up to **\$1,000,000** each in direct costs for up to four years. Indirect (F&A) costs are paid at the appropriate federally approved F&A rate for non-UC Institutions and at 25% for University of California campuses.

Completed responses to this RFP are due by the deadline: noon, April 8, 2016. Signed face pages of submitted applications must be emailed to RGPOgrants@ucop.edu by **5pm Friday, April 8, 2016**. The project start date is **August 1, 2016**.

For more information and technical assistance, please contact:

Katherine McKenzie, Ph.D.

CBCRP Phone: (510) 987-9884

CBCRP Toll free: (888) 313-2277

Background/Justification

Biomarkers have been developed and used in clinical settings to manage the treatment of breast cancer patients for years; however, comparable tools to guide breast cancer prevention have lagged. In addition, research into breast cancer biomarkers has thus far not considered exposure to environmental chemicals as a target.

A definition of a biomarker is a biological parameter that can be measured and evaluated as an indicator of normal or pathological processes, including exposure to environmental factors, and developmental status.¹ Changes to protein, peptide or gene expression profile, gene mutations genes and epigenetic changes such as DNA methylation are examples of the kinds of biomarker alterations that can be occurring in response to exposure to risk factors. The majority of the current biomarkers for risk assessment depend on identifying the genetic germline mutations in genes such as BRCA1/2 and PALB2², although they are relevant to only a small percentage of individuals and the preventive solutions (e.g., mastectomies, oophorectomies, frequent screening) cause substantial morbidity and effects on quality of life. Very little research has been done to identify biomarkers of exposures to known and suspected mammary gland carcinogens, mammary gland toxicants, endocrine disruptors, and/or chemicals with similar properties or similar mechanisms of action.

In the continuum from health to disease, there are many untapped opportunities to identify biomarkers of healthy breast, disease susceptibility and biological changes that indicate increased risk of cancer. For instance:

- Developmental biomarkers in animal studies have shown that prenatal exposure to endocrine disruptors, (e.g., atrazine) result in changes in mammary gland morphology that are associated with increased susceptibility to mammary tumors, but the mechanistic pathway is not fully understood. What other chemicals have these effects? How could we assess this type of effect in humans? How do these changes act to alter breast cancer susceptibility?
- Ongoing investigations aim at identifying markers of chemical exposure. Specifically, what are the biological pathways activated by chemicals known or suspected to be mammary gland carcinogens, mammary gland toxicants, endocrine disruptors, and/or chemicals with similar properties or similar mechanisms of action?
- What are the molecular, tissue, hormonal or other biological 'signatures' that characterize women who have been exposed to an established breast cancer risk factor or protective factor, and can we use the same biomarkers to identify chemical exposures that result in similar changes?

If we are able to develop biomarkers along the pathway from health to breast cancer, these biomarkers can be used to identify exposures that contribute to risk, inform people about their risk, evaluate the effectiveness of preventive interventions, and target interventions to those who will benefit.

There have been many studies that can inform directions for biomarker development. Currently known modifiable events associated with preventable higher risk of breast cancer in women include radiation therapy, reproductive history, decreased pre-menopausal body weight, increased post-menopausal body weight, lack of physical activity, alcohol and tobacco use, the pharmaceutical synthetic estrogen diethylstilbestrol (DES),³ and combination hormone replacement therapy, among others.^{4,5} Epidemiological data have also shown that exposure to the pesticide DDT^{6,7} prenatally and during girlhood increased the risk of breast cancer. In addition, exposure to volatile organic compounds (VOC) is being investigated as a potential cause of breast cancer in men that have worked or lived in a military facility with VOC-contaminated drinking water; this association is supported by evidence of increased breast cancer risk among premenopausal women with occupational VOC exposure and increased mammary tumors in rodent models following solvent/VOC exposure.^{8,9} Several studies have shown higher risk among women with certain genetic variants in combination with exposure to PCBs or PAHs.^{9,10} Mounting toxicology data also link chemical exposure to altered development of the mammary gland and mammary tumor formation, including evidence of effects when exposures occur during gestation.^{11,12} Future research can identify biomarkers that characterize the biological changes that underlie these observations from human and animal studies.

In addition, intermediate biomarkers that are under investigation can serve as a basis for identifying biomarkers of exposure to known or suspect mammary carcinogens. For example, the intermediate biomarker, breast density has been associated with breast cancer risk; women with higher density are estimated to have a 4- to 6- fold increased risk of breast cancer compared to women with lower density.^{13,14} Others have postulated that mammographic texture pattern is affected by endogenous hormone exposure and therefore can predict breast

cancer risk.¹⁵ Using intermediate human biomarkers and developing new ones can provide noninvasive ways to identify high-risk individuals and evaluate effects of exposures or interventions in a shorter timeframe, without waiting for disease to occur.

Recent animal data indicate that epigenetic¹⁶ and metabolic changes,¹⁷ and differential mRNA expression¹⁸ may provide useful upstream biomarkers of exposure to mammary gland toxicants. In vitro breast cell cultures have been used to identify proteins and metabolic pathways that may be uniquely expressed during cancer progression.¹⁹ Recent data using umbilical cord serum from infants born to mothers with pre-eclampsia showed that they have a different proteomic profile compared to those born to mothers without pre-eclampsia.²⁰ Pre-eclampsia is associated with a lower risk of breast cancer in the daughters of the affected pregnancy.²¹ Umbilical cord serum analysis may define how other early-life exposures to chemicals such as endocrine disruptors affect the risk of developing breast cancer later in life.

Ongoing research on gut microbiome indicates that it may also be a promising biomarker of risk. Recently published work by Fuhrman and colleagues²² on healthy postmenopausal women showed that women with a more diverse fecal microbiota had an elevated urinary ratio of estrogen metabolites to parent estrogens. Elevated levels of estrogen are associated with increased postmenopausal breast cancer risk; lowering its level by increasing metabolism (which increases the metabolites to estrogen ratio) has been associated with lower risk.²³

To address the knowledge gaps about biomarkers of health and risk of developing breast cancer, a tailored research approach is needed. The research needs to be transdisciplinary, integrating in vitro, animal and human evidence, with special emphasis on innovative targets and methodology, innovative use of bodily materials that do not require invasive collection procedures, and research on samples that already exist in biobanks. The ultimate goal is to identify early markers of high risk of developing breast cancer over a lifetime in order to create targets for preventive intervention, and identify outcome markers to evaluate the effects of exposures to known and suspected mammary gland carcinogens, mammary gland toxicants, endocrine disruptors, and/or chemicals with similar properties or similar mechanisms of action. New tools will make it possible to assess risk and prevention without waiting 60 years to discover the impact of exposures, to, for example, DES, to result in manifest disease.

There has been a wealth of research on biomarkers for breast cancer, but work on biomarkers of exposures to known or suspected mammary gland carcinogens, mammary gland toxicants, endocrine disruptors, and/or chemicals with similar properties or similar mechanisms of action is scarce. The research funded by this initiative aims to fill that gap.

Research Aims

The goal of this initiative is to pursue innovative approaches using tissue culture, animal models, or human samples to identify and characterize novel biomarkers of breast cancer susceptibility or risk that have the potential to identify individuals (or communities) with high risk and inform intervention strategies to lower risks.

The research aims are to:

1. enhance our understanding of the changes in biological pathways in response to

chemical exposures that decrease or increase risk of developing breast cancer

2. identify and characterize biomarkers of risk of developing breast cancer related to exposures to environmental chemicals that may be used to differentiate high and low-risk women and allow us to target and evaluate prevention strategies

Project Guidelines and Example Research Topics

Proposals that are responsive to this RFP will investigate upstream biomarkers of breast cancer risk and identify novel biomarkers of previous exposure to chemicals known or suspected to be mammary gland carcinogens, mammary gland toxicants, endocrine disruptors, and/or chemicals with similar properties or similar mechanisms of action.

Project Guidelines

1. Projects must focus primarily on markers of risk from chemical exposures. Chemicals relevant to breast cancer are defined for the purpose of this project as: known and suspected mammary gland carcinogens,²⁴ mammary gland toxicants,^{25,26} and/or endocrine disrupting chemicals.²⁷ Other chemicals may be included if their relevance to breast cancer is discussed and justified.
2. Biomarkers of interest include measures of DNA methylation, gene expression, receptor/hormone levels and activity, metabolomics and other indicators of biological change along the pathway from health to breast cancer. If invasive biomarkers are included, methods to demonstrate their relationship with noninvasive methods are encouraged.
3. Research should exclude clinical biomarkers used for tumor characterization, prognosis, disease progression and treatment decisions, unless there is strong scientific support that the candidate marker could also be used as a risk indicator for prevention.
4. Projects that use cell-based and animal toxicology studies should address the relevance to humans and include methods to demonstrate relevance, if needed. The rationale for the relevance of experimental dose levels to human exposures should be integrated into the research design.
5. Projects are encouraged to include transdisciplinary research collaboration and must include collaboration with advocates and community stakeholders. CBCRP staff members are available to advise applicants about community collaborations.

Transdisciplinary research is defined as research that is focused on solving a problem that crosses traditional disciplinary boundaries. Transdisciplinary projects may include integrating laboratory and population level studies or collaboration across fields such as genetics, biochemistry, epidemiology, physiology, sociology, biostatistics, oncology, toxicology, image analysis, and community-based participatory research.

Example research topics

1. Identify biomarkers of the effect caused by exposures to breast cancer-relevant chemicals singly or in mixtures in experimental models (e.g., rodent or in vitro tissue culture models). A critical period of mammary gland development should be represented in the experimental design. Projects should seek to identify biological pathways connecting exposure to risk biomarkers and to altered incidence of tumors (for examples see Gohlke et al., 2009²⁷ and Sturla et al 2014²⁸). Projects that extend *in vitro* and *in vivo* experimental findings into humans are most responsive to the RFP.
2. Identify biomarkers of the effects of chemical exposures in high versus low risk women. Low- and high- risk classification could be based on criteria such as reproductive history, gene mutations, family history of breast cancer or work history.
3. Develop biomarkers of the cumulative effect of chemical mixtures.
4. Develop experimental models to test for mammary tissue alterations (e.g. breast cells, connective tissue) due to chemical exposure and relate these changes to circulating biomarkers that could be of cellular, epigenetic, proteomic or metabolic origin and can be investigated in humans.
5. Evaluate changes in a relevant biomarker following an intervention or natural change in chemical exposure.

Budget

Applicants should consider the following elements when constructing their budgets:

- **Expertise:** Proposals must involve researchers with appropriate proficiency for the research questions (e.g. epidemiologist, breast cancer biologist, statistician, toxicologist)
- **Capacity:** Applicants should demonstrate possession of or access to appropriate tools and technologies (e.g. laboratory facilities and equipment, animal facilities, etc.)

Details on allowable costs can be found in section *Budget Summary* section on page 17 of this RFP.

References

¹ Schrohl *et al.* Banking of Biological Fluids for Studies of Disease-associated Protein Biomarkers. 2008. *Molecular & Cellular Proteomics* 7: 2061–2066

² Antoniou *et al.* Breast-Cancer Risk in Families with Mutations in PALB2. 2014. *New England Journal of Medicine*. Published online August 7. DOI: 10.1056/NEJMoa1400382

³ Hoover *et al.* Adverse Health Outcomes in Women Exposed In Utero to Diethylstilbestrol. 2011. *New England Journal of Medicine* 365:1304-1314

⁴ Rudel *et al.* New Exposure Biomarkers as Tools for Breast Cancer Epidemiology, Biomonitoring, and Prevention: A Systematic Approach Based on Animal Evidence. 2014. *Environmental Health Perspective*. Published online May 12.

⁵ Institute of Medicine of The National Academies. Breast Cancer and the Environment: A Life Course Approach. 2011. See <https://iom.nationalacademies.org/Reports/2011/Breast-Cancer-and-the-Environment-A-Life-Course-Approach.aspx>

- ⁶ Cohn *et al.* DDT and breast cancer in young women: New data on the significance of age at exposure. 2007. *Environmental Health Perspectives* 115(10):1406-1414.
- ⁷ Agency for Toxic Substances and Disease Registry. Male breast cancer study. 2014. See <http://www.atsdr.cdc.gov/sites/lejeune/MaleBreastCancerStudy.html>
- ⁸ Brody *et al.* Environmental pollutants and breast cancer: epidemiologic studies. 2007. *Cancer* 109:2667-2711
- ⁹ Ekenga *et al.* Breast cancer risk after occupational solvent exposure: the influence of timing and setting. 2014. *Cancer Research* 74:3076-3083
- ¹⁰ Rudel *et al.* Environmental Exposures and Mammary Gland Development: State of the Science, Public Health Implications, and Research Recommendations. 2011. *Environmental Health Perspective* 119:1053-1061
- ¹¹ Birnbaum LS, Fenton SE. Cancer and developmental exposure to endocrine disruptors. 2003. *Environmental Health Perspectives* 111:389–394.
- ¹² Razzaghi *et al.* An association between mammographic density and basal-like and luminal A breast cancer subtypes. 2013. *Breast Cancer Research* 15:R76
- ¹³ McCormack and dos Santos Silva. Breast Density and Parenchymal Patterns as Markers of Breast Cancer Risk: A Meta-analysis. 2006. *Cancer Epidemiol Biomarkers Prev* 15:1159-1169
- ¹⁴ Daye *et al.* Mammographic parenchymal patterns as an imaging marker of endogenous hormonal exposure: a preliminary study in a high-risk population. 2013. *Acta Radiologica* 20:635-646
- ¹⁵ Dhimolea *et al.* Prenatal Exposure to BPA Alters the Epigenome of the Rat Mammary Gland and Increases the Propensity to Neoplastic Development. 2014. *PLoS ONE* 9(7): e9980
- ¹⁶ Cabaton *et al.* Effects of Low Doses of Bisphenol A on the Metabolome of Perinatally Exposed CD-1 Mice. 2013. *Environmental Health Perspectives* 121:586–593
- ¹⁷ Wadia *et al.* Low-Dose BPA Exposure Alters the Mesenchymal and Epithelial Transcriptomes of the Mouse Fetal Mammary Gland. 2013. *PLoS ONE* 8(5): e63902
- ¹⁸ Shaw *et al.* Integrated Proteomic and Metabolic Analysis of Breast Cancer Progression. 2013. *PLoS ONE* 8(9): e76220
- ²⁰ Low *et al.* Screening preeclamptic cord plasma for proteins associated with decreased breast cancer susceptibility. 2013. *Genomics Proteomics Informatics* 11:335-344
- ²¹ A. Ekblom, C.C. Hsieh, L. Lipworth, H.O. Adami, D. Trichopoulos. 1997. Intrauterine environment and breast cancer risk in women: a population-based study. *J Natl Cancer Inst* 89: 71–76
- ²² Fuhrman *et al.* Associations of the Fecal Microbiome With Urinary Estrogens and Estrogen Metabolites in Postmenopausal Women. 2014. *Journal of Clinical Endocrinology and Metabolism*. Published online September 11. jc20142222.
- ²³ Rudel *et al.* have identified 216 chemicals that have been associated with increases in mammary gland tumors in at least 1 animal study. See: Rudel RA, Attfield KR, Schifano JN, Brody JG. Chemicals causing mammary gland tumors in animals signal new directions for epidemiology, chemicals testing, and risk assessment for breast cancer prevention. 2007. *Cancer* 109:2635-66.
- ²⁴ Mammary gland toxicants include commercial chemicals or pharmaceuticals reported to induce morphological or functional change in the mammary gland, including but not limited to: high production/exposure chemicals such as chlorotriazine metabolites, perfluorinated compounds, parabens and BPA replacements.
- ²⁵ Rudel *et al.* Environmental Exposures and Mammary Gland Development: State of the Science, Public Health Implications, and Research Recommendations. *Environmental Health Perspectives* 119:1053-1061.
- ²⁶ <http://endocrinedisruption.org/endocrine-disruption/tedx-list-of-potential-endocrine-disruptors/overview>
- ²⁷ Gohlke *et al.* Genetic and environmental pathways to complex diseases. 2009. *BMC Systems Biology* 3:46. doi: 10.1186/1752-0509-3-46.
- ²⁸ Sturla *et al.* Systems Toxicology: From Basic Research to Risk Assessment. 2014. *Chemical Research in Toxicology* 27:314-329

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. Are the concepts and hypotheses speculative and exploratory? Are methods novel and original? Has(ve) the investigator(s) thought creatively about the choice chemicals or mixtures to be examined and the experimental models and/or populations to be studied? Is the research team transdisciplinary?
- **Impact:** Potential for the project, if successful, to identify new biomarkers for assessing chemical exposures. Will the research generate new approaches or markers that can be used to target and evaluate prevention strategies?
- **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 template

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 Additional Criteria template provides a convincing argument that the proposed research has the potential to inform the development and/or implementation of California chemicals policy.
- **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?
- **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?

Application Process and Instructions

Submission Deadline: Applications must be submitted through proposalCENTRAL (<https://proposalcentral.altum.com/>) by **Friday, April 8, 2016 at 12 noon Pacific Standard Time.**

Signed face pages of submitted applications must be emailed to RGPOgrants@ucop.edu by 5pm on **Friday, April 8, 2016.**

The application materials will be available on proposalCENTRAL by **December 1, 2015.**

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 the CBCRP to reject and return the submission without peer review.

Online Application (Proposal) Management

The 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 on Friday, April 8, 2016.** *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 PI 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 Biomarkers 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.

Title Page

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 August 1, 2016. Enter the end date of the project (up to 4 years).

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.

Enable Other Users to Access this Proposal

Note: A person must be registered in proposalCentral before s/he can be given access. Read the instructions on this page thoroughly to understand the different levels of access. 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 RFP, then click “Find User.” Select the desired level of access and Click “Accept Changes” to save.

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.”

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.

Abstracts

Copy each the Lay Abstract and the Scientific Abstract from the CBCRP templates into the appropriate boxes on the proposalCENTRAL page. **Note:** symbols or other special text will not copy.

On this page you should also select and add CSO codes. At <https://www.icrpartnership.org/CSO.cfm> you will find the seven major CSO categories, each with 4-9 sub-categories. 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.

Budget

Provide the total costs for the entire funding request for each 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.

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”.

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 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.

ORCID ID number

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.

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.”

Print Face Page When Application Complete

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

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.

Email Face Page Submission

The PI, 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 Friday, April 8, 2016.

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 your 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 and by the CBCRP Council/SRI Steering Committee (see www.cabreastcancer.org/funding-opportunities/sri).

CBCPI Focus: 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.

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 interventions, policy and/or other practice.

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 limitations, age, occupation and/or other factors)?

Advocacy Involvement (REQUIRED)

This item is evaluated in the programmatic review. Follow the instructions on the form, and 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.

Letter(s) of Commitment (REQUIRED)

This item is evaluated in the programmatic review. 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 direct costs of an individual award are capped at \$1,000,000. The maximum duration may not exceed 4 years.

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 each CBCPI 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).

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 CBCPI 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* four (4) 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 content:

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 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 and policy analysis.

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 Grant Application #398 http://grants2.nih.gov/grants/peer/tree_glossary.pdf. Most research projects funded by the CBCRP falls into Exemption category #4. Although 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 the 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 the CBCRP as soon as possible, but **no later than August 1, 2016**. Funds will not be released until all assurances are received by the 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 NICI 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. The CBCRP may require documentation that a DSMB is in place or planned prior to the onset of the trial.

Vertebrate Animals (OPTIONAL)

This item is evaluated in the peer review. **This form is required only for applications that use Vertebrate Animals. Limit the text to two pages.**

If you have answered “**YES**” to the Vertebrate Animals item on the Organizations Assurances section of the CBCPI Application Face Page, then following **five points** must be addressed. When research involving vertebrate animals will take place at collaborating site(s) or other performance site(s), provide this information before discussing the five points.

1. Provide a detailed description of the proposed use of the animals in the work outlined in the Research Plan. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.

2. Justify the use of animals, the choice of species, and the numbers used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.
3. Provide information on the veterinary care of the animals involved.
4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic and tranquilizing drugs, and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.
5. Describe any methods of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. If it is not, present a justification for not following the recommendations.

Documentation of Assurances for Vertebrate Animals

Grants will not be awarded for research involving vertebrate animals unless the program for animal care and welfare meets the standards of the AAALAC or the institution has a U.S. Public Health Service assurance. In the appendix, if available at the time of submission, include official documentation of institutional review committee approval showing the title of this application, the principal investigator's name, and the inclusive approval dates. Do not include supporting protocols. Approvals obtained under a different title, investigator or institutions are not acceptable unless they cross-reference the proposed project. If review is pending, final assurances should be forwarded to the CBCRP as soon as possible, but **no later than August 1, 2016**. Funds will not be released until all assurances are received by the CBCRP.

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 22 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 22 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 the 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

The 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 the 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 the 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 June 30, 2016. 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 the 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) Executive Director Dr. Mary Croughan. 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 the 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>.