Request for Proposals (RFP)
Pilot Studies to Examine Hormone Concentrations of Interest to Breast Cancer Risk in California's Beef and Well Water

California Breast Cancer Research Program
California Breast Cancer Prevention Initiatives

Deadline to apply
December 5, 2019

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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.

Pilot Studies to Examine Hormone Concentrations of Interest to Breast Cancer Risk in California's Beef and Well Water

A paucity of information is publicly available regarding the human food safety evaluations that form the scientific basis for Food and Drug Administration (FDA) animal drug approvals, especially for hormones. Limitations in industry and federal approaches to evaluation make it difficult to form a comprehensive picture of residues in retail animal products. Insights into cumulative exposure burdens of Californians may be gained from analysis of samples of retail consumer beef as well as private well water samples. Data documenting drinking water hormone exposure could serve as a first step towards epidemiologic investigations examining the impact of these exposures on subclinical (or clinical) outcomes in follow-up research. This initiative aims to fund two pilot studies, each looking at a different avenue of exposure resulting from beef production.

Available Funding

This initiative aims to improve our understanding and quantify exposures to various concentrations of both endogenous and exogenous hormones of interest for breast cancer risk resulting from food animal production by sampling beef and well water.

CBCRP intends to fund two types of projects under this initiative:

- Project I (Hormones in Beef): One pilot project to characterize the presence of seven FDA approved drugs in beef products sold in California.
- Project II (Hormones in Well Water): One pilot project to characterize the presence of seven FDA approved drugs for use in beef production in California's well water.

Each type of project has a maximum direct cost budget of $200,000 and duration of 2 years.

Completed responses to this RFP are due by the deadline: December 5, 2019. The project start date is June 1, 2020.

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Background/Justification

Toxicological and residue assessment of hormones are supported primarily by industry studies that are not made available to independent scientists for review; as a result, it is impossible to assess the quality and strength of the evidence on which FDA bases its safety decisions. Federal approaches to hormone residue testing are also inadequate for assessment of human exposure. A small, changing number of compounds are inconsistently tested from year to year. The tests rely on potentially outdated methods and do not permit longitudinal evaluation of residue levels in animal products. A search of the open literature indicates that representative studies of residues in retail animal products are lacking.

Limited transparency from the FDA regarding exposures from drug residues and major gaps in the literature provides for novel research opportunities to improve understanding and quantify exposures to various concentrations of both endogenous and exogenous hormones of interest for breast cancer risk from food animal production. Analysis of private well water samples for these compounds will provide a novel portrait of the cumulative exposure burdens faced by California residents who rely on these sources for drinking water. Further, data documenting drinking water hormone exposure could serve as a first step towards epidemiologic investigations examining the impact of these exposures on subclinical or clinical outcomes in follow-up research.

The data from the pilot study could advance, or rule out the need for, larger studies that characterize hormone residue levels in food and water which in turn could inform independent toxicological studies that examine the biological significance (if any) of long-term, low-dose hormone exposures through diet, especially during critical life-stages, and tell us what the use of approved drugs means in terms of subsequent dietary exposure that may have important implications for breast cancer prevention. Thus, this pilot study would serve as a first step towards understanding the potential impacts of these animal production practices on human health.

I. Drug/Hormones Used in Food Animal Production

In recent years, increasing attention has been paid to various sources of hormones that may be involved in breast cancer etiology following reports that heightened levels of endogenous hormones and exposure to exogenous hormones and other endocrine-disrupting chemicals in food are associated with increased breast cancer risk.[1,2,3] In the U.S., seven pharmaceutical compounds approved by the FDA for use in food animal production are either endogenous hormones (i.e., testosterone propionate [TP], estradiol [E2] and estradiol benzoate, and progesterone) or compounds that display high affinities for human hormone receptors (i.e., trenbolone acetate [TBA], zeranol, and melengestrol acetate [MGA])[4] (Table; NL = non-lactating dairy cattle BS = breeding stock). These drugs are approved for use in cattle and, in the case of zeranol, sheep to increase weight gain and improve feed efficiency (two related indications generally known as “growth promotion”).

E2, progesterone, and MGA are also approved to manage estrus in beef cattle and sheep. An additional compound, bovine somatotropin (bST) is approved for use in dairy cattle to increase milk production. bST is known in some cases as recombinant bovine somatotropin [rBST], bovine growth hormone [bGH], or recombinant bovine growth hormone [rBGH]. Hormones are not approved for use in poultry or swine.

Table. FDA-Approved Hormones for Use in Food Animal Production

Active Ingredient	Beef	Dairy	Sheep
Estradiol	x	NL	
Melengestrol acetate	x		
Progesterone	x	BS	x
bST		x	
Testosterone propionate	x		
Trenbolone acetate	x		
Zeranol	x		x

There is concern that the drugs used in cattle and sheep or their biologically active metabolites may accumulate in edible tissues or dairy products from treated animals, potentially exposing consumers of these products.[5] There is also concern that bST use in dairy cattle increases levels of an endogenous hormone, insulin-like growth factor 1 (IGF-1), in milk and dairy products, likewise exposing consumers.[6] As a result, use of these drugs has been controversial. The U.S. and European Union (EU) governments have engaged in a decades-long trade dispute over importation of U.S. beef from cattle that received them.[7] The question of whether or not the use of one or more of these drugs poses a human health risk remains subject to debate.[5,7]

The debate on hormones in food is fueled in part by formidable data gaps in understanding toxicity, exposure and ultimately the potential health risk of hormones in food. The quantitative risk assessment process developed by a National Research Council (NRC) committee in 1983 is the standard approach to estimating human health risks posed by chemical exposures.[8] A variant of this process has been adopted by the FDA for evaluation and approval of new animal drugs for use in food animal production.[9] The NRC process consists of four steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization.[8] The published literature is very limited on each of these factors. However, extensive testing by sponsors is performed and study reports and raw data are submitted to regulatory agencies like the FDA and international bodies like the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Following FDA approvals, however, only brief Freedom of Information (FOI) summaries of the industry-submitted

studies may be available, making an independent assessment of the data and conclusions difficult or impossible.

In light of our current knowledge of the association between exposure to endogenous and exogenous hormones and breast cancer risk, widespread exposure to animal food products, and a lack of published, independent research on which to evaluate risk, further characterization of exposure to hormones in food can contribute greatly to advancing prevention-based interventions for breast cancer.

II. Toxicity

Chronic (especially lifetime) bioassays of oral toxicity of the seven compounds (Table) in the published literature are largely lacking. While evaluations of these compounds, sponsored by drug manufacturers, are submitted to the FDA as part of the new animal drug application process, they are not made available to the public for independent evaluation. Thus, they cannot be used to estimate risks and related burdens for people consuming animal products. The extant literature primarily utilizes subcutaneous dose delivery, in which the bioavailability of the administered dose approaches 100%.

This route does not account for variation in toxicological parameters that may result from differences in bioavailability or metabolism of compounds following oral exposure. In addition, the endpoints assessed in the published literature generally do not reflect an emerging understanding of the importance of upstream markers (e.g., circulating hormone levels) on subsequent clinical disease (e.g., breast cancer) nor do they address our current understanding of the importance of whether the exposure occurs during critical or sensitive periods of human development.

III. Exposure

Human exposure to hormones from consumption of animal products is primarily a function of residues present in food in retail markets and consumption of meats, milk and egg products. Available data streams for residue levels include: (1) New Animal Drug Applications (NADA); (2) U.S. National Residue Program; and (3) Published research.

Nationwide dietary intake data for animal products are available through the What We Eat in America (WWEIA) dietary survey of the National Health and Nutrition Examination Survey (NHANES).[10,11] There are many limitations to these sources of exposure information. Moreover, there appear to be no California-specific data related to hormone residues in animal products and there are no animal product consumption data specific to California. An additional consideration in understanding exposure to hormones used in food animal production is consumption of drinking water from household wells impacted

by effluent from meat and dairy production facilities. Each of these aspects of exposure is described below.

III.A. Residues

New Animal Drug Applications. For hormones administered to food animals, data from feeding studies that show the rates of depletion of these compounds in the edible tissues of dosed food animals are required to be generated by drug companies (known as "sponsors") as part of an NADA submitted to the FDA to obtain approval for legal marketing. As part of the drug approval process, the sponsor of a new animal drug is required conduct and submit studies to the FDA that characterize residues that may persist in animal products when the drug is used in accordance with the conditions of use proposed in the NADA. These studies are used to inform recommended dosages and to set withdrawal periods (i.e., the number of days before slaughter that use of the drug must end) that are intended to ensure that remaining residue concentrations have fallen to levels the FDA considers "safe" for human consumption. If properly conducted, these residue studies could be especially helpful in efforts to characterize population exposures to residues through consumption of animal products.

Despite the promise they may hold, the reporting of these studies can be flawed and public accessibility is often limited. The study reports are not released to the public; rather, FOI summaries that contain brief descriptions of the studies submitted have been prepared for approvals granted since 1975. For some hormonal drugs, FOI summaries are not available online. Assuming the approval in question occurred in 1975 or later and a FOI summary was prepared, it must be acquired through a formal Freedom of Information Act request, a process that can be lengthy.

Among synthetic hormones approved for use in food animal production, FOI summaries that include substantive toxicological reviews are not available for zeranol (first approved in 1969) or MGA (first approved in 1968).[12] Melengestrol acetate was introduced as a food additive, just before the process for "new animal drugs" was established in 1968 by amendment to the Federal Food, Drug and Cosmetic Act; thus, no original NADA was identified. It is possible that the drug was "grandfathered" into the system, thus explaining a lack of identifiable toxicological review. Trenbolone acetate was first approved in 1987, and has a FOI summary with a substantive toxicological evaluation that was last updated in 1996.[13] Similarly, a FOI summary (with a toxicological review) is available for rBST, which was last evaluated in 1993.[14]

For externally administered endogenous hormones, researchers at Johns Hopkins were unable to locate FOI summaries with toxicological reviews for progesterone, E2 and testosterone. In some FOI summaries for E2 and testosterone (as they are part of numerous combination approvals and dosage forms), the agency states that it "has concluded that no harmful effects will occur in individuals chronically ingesting animal

tissues that contain an incremental increase of endogenous steroid equal to 1% or less of the amount produced daily by the segment of the population with the lowest daily production."[15] No explanation or rationale is provided for the selection of a 1% increase, and the FOI summaries state that if drug sponsors can demonstrate that residues in meat will result in exposures less than the permitted increase, then the drugs are considered safe.

Even for drugs where residue depletion summaries are easily accessible, problems with data design and results reporting limit confidence in any conclusions. An example can be found in the case of NADA 141-043, for a combination implant drug containing TBA and estradiol benzoate.[16] In the FOI summary associated with this approval, serious issues are apparent regarding study design (i.e., data from half [heifers] of the 24 animals tested were dropped, leaving only 12 animals [steers] with unspecified exposure group assignment) and reporting clarity (i.e. number of animals per group is not reported, no control data are reported, urinary and fecal residue measurements are not reported) that would challenge the value of this study for determination of anticipated residues. In this particular case, this study was used to support the decisions to not require marker residue tolerances or withdrawal periods for the drug. Feeding studies conducted outside of the NADA process are not common, but some have found measurable residue concentrations in edible tissues.

U.S. National Residue Program. Another potential source of residue data within the US is the National Residue Program (NRP, which is administered by the Food Safety and Inspection Service of the USDA). The NRP is the only federal effort that routinely examines animal products for residues of administered drugs. An examination of the testing regimens of the NRP from 2002 to 2012 indicates that only three hormones (MGA, TBA and zeranol) have been examined at all during that surveillance period.[17-27] No hormone residue monitoring data were collected under the NRP in 2011 and 2012, though the NRP has noted it has scheduled zeranol and MGA for 2013 sampling efforts[28]; previous years saw variability in which of these three hormones were monitored. For each drug, only a single tissue was tested in the monitoring program. Heifer fat was the tissue analyzed in the case of MGA, whereas livers from formula-fed and non-formula-fed veal calves were the sole tissue examined for both TBA and zeranol. From 2002 – 2012, the greatest number of hormone residue tests was conducted in 2005, and subsequent years saw a steady decline in the number of samples tested.

The NRP does not report hormone residue concentrations as continuous variables. Instead, they are reported as binned categories based on the concentrations detected. Over the period examined, some violations of residue tolerances were observed for zeranol and TBA. In 2002, 16% of samples tested were in violation of residue tolerances. Violations dropped to 5% in the following year (2003), though zeranol was excluded from NRP analysis in 2004.

Challenges exist in utilization of NRP data for the purpose of understanding dietary exposures to hormones in the US population. Testing for hormones is performed in tissues not commonly consumed by people, which would require extrapolations to estimate concentrations in animal products like muscle tissue and milk. Further, residue data reporting is extremely crude and would not allow for the construction of residue concentration distributions or descriptive statistics. Many of these shortcomings are likely a result of the core conflict between the purpose of the NRP and the needs for exposure assessment, as the primary purpose of the NRP – the removal of animal products with residue levels in violation of the regulations from the food supply – may require different data than what is needed to understand residue exposures in people.

Published Literature. While the literature describing various techniques for determination of hormone residues in animal products is expansive, few studies have identified residues in retail animal products. To date, the largest literature is available for hormone residues in dairy products, and studies of E1 and E2 levels in various milk products were most common. The majority of studies identified typically analyzed small numbers of retail samples; single samples per product type were not uncommon, and studies rarely exceeded ten samples per product. Estrogens, particularly forms of E2, were the most frequently examined.[29-34] Looking across studies, some patterns emerge, though it is necessary to acknowledge that the limited number of studies and small sample sizes within those studies do not allow for statements of great certainty.

Research has demonstrated that use of rBST in dairy production has been linked to increases in concentrations of IGF-1 in dairy products from treated animals. Despite this, anecdotal evidence suggests that public concerns related to the use of rBST have prompted dairy producers to abandon the additive, and USDA data suggest that less than a quarter of dairy cows are treated with the drug.[35]

A smaller number of studies have attempted to characterize residues of synthetic hormones in retail beef products.[30,36,37,38] These studies report inconsistent results with some lacking clear descriptions of analytical and/or meat-sourcing methods providing limited confidence in (and relevance of) the findings.

III.B. Consumption

The What We Eat in America (WWEIA) dietary survey analyzed by the EPA and reported by product as per capita or consumers-only intake rates in the 2011 Exposure Factors Handbook (EFH)[39] are the best estimates suited for use in estimation of hormone exposure through foods, as they are derived from the most recent synthesis of NHANES dietary data. In some cases, animal product intake rates are reported by life stage (or age grouping) or by race-ethnicity.

The EPA EFH includes some animal product intake data specific to pre-menopausal women. Women between the ages of 13 and 49 consume about 20% less meat on average than the general population, after adjustment for body weight. They also consume just over half of the amount of dairy products that the general population eats. As far as specific meats, women ages 13 - 49 eat about 28% less pork, 22% less beef, and 14% less chicken. While data specific to women ages 50 and over were not available, estimates for people 50+ (for males and females combined) suggest that total meat intake and beef, poultry and dairy product intakes were further reduced below women ages 13-49. Pork intake among persons over 50 was slightly higher than that of women ages 13-49. Data for animal product-specific intake rates for post-menopausal women are needed to estimate dietary hormone exposures in this subpopulation.

Patterns of body-weight adjusted intake of animal products follow a clear pattern. For total meats, and for poultry, dairy products and eggs, per capita body-weight peaks early in life, between ages one and two years. Body weight-adjusted beef and pork consumption peaks between the ages of three and five. Per capita rates of body weight-adjusted intake of dairy products remain elevated until the teenage years at about twice the per capita average.

III.C. Hormones in Well Water Systems in California

In a typical year, California relies on groundwater for approximately forty percent of its water supply, and nearly 16 million California residents use groundwater for their drinking water supply. A sub-set of these residents rely on private wells, which are not subject to federal drinking water regulations. While some states have minimal safety or inspection requirements for private wells, state-level action is usually only triggered during property transfer and rarely requires periodic monitoring of water quality.[40]

A growing body of scientific literature shows that effluent from concentrated animal feeding operations (CAFOs) and manure storage lagoons are capable of contaminating groundwater with a variety of contaminants, including nitrates, pharmaceuticals and hormones.[41-43] California has a sizable dairy industry, with a 2012 inventory of nearly 2 million dairy cattle, that accounts for more than 20% of the US milk production annually. There is also a sizeable beef production industry in the state – California has a 5.2 million head beef cattle inventory. Dairy and beef production occurs primarily in rural settings; thus, waste that is stored in manure lagoons or applied to crop fields as fertilizer may transport manure-borne hormones and other contaminants to groundwater sources used by California residents for drinking water.

Given the size of the dairy and beef industries in California there exists a potential risk for impacting groundwater. In light of the fact that certain regions of California rely on groundwater sources for drinking water, it is important to understand the contribution of dairy and beef (and other animal) production sites to human exposures to hormones.

IV. Health Risk

Key limitations of the currently available data preclude conducting quantitative dose-response and exposure assessments. An early stage of the animal drug approval process is the generation of safety and effectiveness data for a proposed drug by its sponsor. These studies are either conducted or funded by the sponsor, and submitted to the FDA as part of a NADA described above. Included in the data package as part of the NADA submission are toxicological studies to support an assessment of "human food safety" by the FDA's Center for Veterinary Medicine (CVM), which encompasses four main steps: a toxicological evaluation (in which CVM determines an ADI); determination of residues that may result from routine use (in which CVM sets residue tolerances and withdrawal times); a microbiological examination of the impact of the use of the drug on bacteria and resulting resistance; and a determination of the regulatory method, which considers the appropriateness of the testing methods used by the drug sponsor in its human food safety studies.[44]

As above, the studies and primary data submitted to support toxicological evaluations are not available to the public. It is also important to note that in many cases, individual drugs may receive additional approvals for use in new species or in combination with other drugs. While these new uses may serve as an opportunity for CVM to require new toxicological evaluation of specific drug ingredients, it is uncommon for additional testing to be required or submitted. Instead, CVM usually refers to toxicological evaluations conducted as part of earlier approvals for the specific active ingredients, even if these evaluations were conducted decades before.

V. Summary

At present, the available data do not permit an evidence-based quantitative characterization of risks that result from the use of hormonal drugs in food animal production. Thus, despite increased recognition of the role of endogenous and exogenous hormones in breast cancer risk and widespread exposure to food animal products, our understanding of the role of dietary hormone exposure in the population burden of breast cancer is not possible at this time. [45]

In recognition of this research gap, we propose funding one pilot study to test two hypotheses: 1) that there are FDA-approved food animal production drug residues, including suspected mammary gland toxicants, prevalent in edible portions of beef products as well as in well drinking water systems in California; and 2) there are quantifiable naturally occurring/ endogenous hormone concentrations in edible portions of both retail USDA certified organic and conventional beef that may have implications for breast cancer risk. This second hypothesis, based on the fact that pregnant and lactating food animals have high levels of endogenous hormones, would provide

essential complimentary information to our understanding of the contribution of food animal products to exposure to hormonally active compounds of interest to breast cancer risk.

This research would collect the most basic information about hormones in food - whether or not they are even present, and if present, at what levels. There is currently no information concerning hormone residues in meat that can be used to estimate the number of samples needed for a study of hormones in food to have sufficient power to inform conclusions. Specifically, a sense of the variance observed in hormone levels in animal product samples for the various hormones of interest is needed. This pilot project would fill this data gap. This pilot study approach has been successfully employed in studies by researchers at Johns Hopkins of contaminant residues in animal products.

The results provide some insight into expected residues and are used to develop estimates of the number of samples needed to characterize residue occurrence and magnitude with confidence (that will support statistical comparisons). These pilot studies have been especially useful in guiding fuller studies or deciding that a particular project is not worth pursuing on a larger scale.

The results of the pilot study will provide the evidence needed to begin to characterize the nature and extent of FDA-approved food animal production drug/hormone residues in the food and water supply in California as well as of naturally occurring hormones of interest for breast cancer in the food supply. The methods developed for this project can be used in future studies to characterize exposure using more comprehensive testing of food and water. Future studies could utilize raw data from WWEIA (which are publicly accessible) to quantify subsequent dietary exposure for subpopulations of interest for breast cancer, which could elucidate potential disparities in exposure that might contribute to disparities in risk. For example, future studies of levels of hormones in food could be coupled to in-depth analyses of intake rate distributions for subgroups of particular concern in breast cancer prevention efforts. These rates would better support dietary exposure estimation for hormones in vulnerable populations.

Project Guidelines

The main goal of this RFP is to improve our understanding and quantify exposures to various concentrations of both endogenous and exogenous hormones of interest for breast cancer risk resulting from food animal production by sampling beef and well water.

This initiative aims to improve our understanding and quantify exposures to various concentrations of both endogenous and exogenous hormones of interest for breast cancer risk resulting from food animal production by sampling beef and well water.

If more than one project is funded, we expect that the grantees will meet periodically during their project periods to exchange information and preliminary findings. Applicants may apply for one or both of these projects.

PROJECT I

Maximum length of Project I: 2 years
Maximum direct costs of Project I: $200,000

Project I would be a pilot study to **characterize the presence of seven FDA approved drugs in beef products sold in California.** Beef products would be examined for endogenous hormones (testosterone propionate [TP], estradiol [E2] and estradiol benzoate, and progesterone) and synthetic hormones (trenbolone acetate [TBA], zeranol, and melengestrol acetate [MGA]). Samples would be collected from retail stores in the state of California. Beef sampling should evaluate both conventionally produced and USDA-Certified Organic samples for endogenous hormones.

Additional Considerations and Requirements for Project I:

The pilot should include beef samples from:

- various brands, as synthetic hormone use practices may vary across producers
- both USDA certified organic and conventional beef products

In developing a sampling strategy consideration must be given to the fact that the FDA does not require producers to report hormone use practices, nor does it report sales data for synthetic hormone products from pharmaceutical manufacturers. Moreover, product labels do not uniformly facilitate identification of animal products derived from treated animals, since producers have no obligation to report hormone treatment. USDA Organic certification labels, however, are federally regulated, and should only be used on products derived from animals that were not treated with synthetic hormones (MGA, TBA and zeranol in beef). Products that do not bear the USDA Organic certification label do not provide insights as to hormone use – it is possible (but not guaranteed) that one or more hormones could have been employed in the production of those animals.

The use of synthetic hormones is believed to be common in the beef industry. In some cases, conventional producers will label their products as being produced without the use of synthetic hormones. With this in mind, it is possible to target sample analyses to reflect likely usage in the industry.

PROJECT II

Maximum length of Project II: 2 years
Maximum direct costs of Project II: $200,000

Project II would be a pilot study to **characterize the presence of seven FDA approved drugs for use in beef production in California's well water**. This study would examine the same seven drugs as in Project I: endogenous hormones (testosterone propionate [TP], estradiol [E2] and estradiol benzoate, and progesterone) and synthetic hormones (trenbolone acetate [TBA], zeranol, and melengestrol acetate [MGA]). The research would be conducted in a cross-section of California households at potential risk of contamination due to effluent from large-scale animal production and dairy facilities. Depending on the results, these data could be paired with geo-referenced data on animal production sites, which would allow for analyses of spatial relationships between animal production and groundwater contamination with hormones.

Additional Considerations and Requirements for Project II:

It is critical that an understanding of the locations of animal production and manure spreading inform selection of sites/water sources from which samples are acquired, to ensure characterization of hormone contaminant profiles in water can be linked to surface activities.

Sampling of water should include sources of ground or surface waters used as drinking water, preferably from private wells or monitoring wells to which a local or state environmental agency may have access.

The study should include both synthetic and endogenous hormones, depending on the spatial and hydrogeological relationships that exist between animal production sites and sources of water used for human consumption.

Budget

CBCRP intends to fund 2 pilot projects, each with a maximum direct cost budget of $200,000 and duration of 2 years.

- Project I (Hormones in Beef): One pilot project to characterize the presence of seven FDA approved drugs in beef products sold in California.
- Project II (Hormones in Well Water): One pilot project to characterize the presence of seven FDA approved drugs for use in beef production in California's well water.

Indirect (F&A) costs are paid at the appropriate federally approved F&A rate for all institutions except for University of California campuses, which receive a maximum of 30% F&A (26% for off-campus projects).

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, endocrinologist, toxicologist, chemist)
- Capacity: Applicants should demonstrate possession of or access to appropriate tools and technologies (e.g. laboratory facilities and equipment, animal facilities, etc.)

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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 hormones in beef (Project I) or well water (Project II). 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 hormones?

- **Impact:** Potential for the project, if successful, to change policy for or regulation of hormone use in beef production. Does the research have the ability to translate to population-level change? Will the data yielded by the research be 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 Program Responsiveness 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 Program Responsiveness form provides a convincing argument that the proposed research has the potential to inform the development and/or implementation of beef production 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?

- **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 Involvement forms.]

Application Process and Instructions

SmartSimple Submission Instructions

Submission Deadline: Applications must be submitted through SmartSimple (https://ucop.smartsimple.com/) by **Thursday, December 5, 2019 at 12 NOON Pacific Standard Time**.

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 3/4 inch.
- PI last name and first name 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: SmartSimple. Following are instructions on how to register and how to submit your response to the RFP. The submission deadline is December 5, 2019. Please consult with your local C&G office for campus submission requirements, and allow enough time to meet submission deadlines. **Note: New to this cycle, all signatures will be collected electronically. You will submit the application electronically to your signing official who must review and submit the application through SmartSimple by the application deadline. Please plan submission timelines accordingly.**

If you have any problems using SmartSimple, please contact the RGPO Contracts & Grants application support line at (510) 987-9386, option 1.

Online Registration

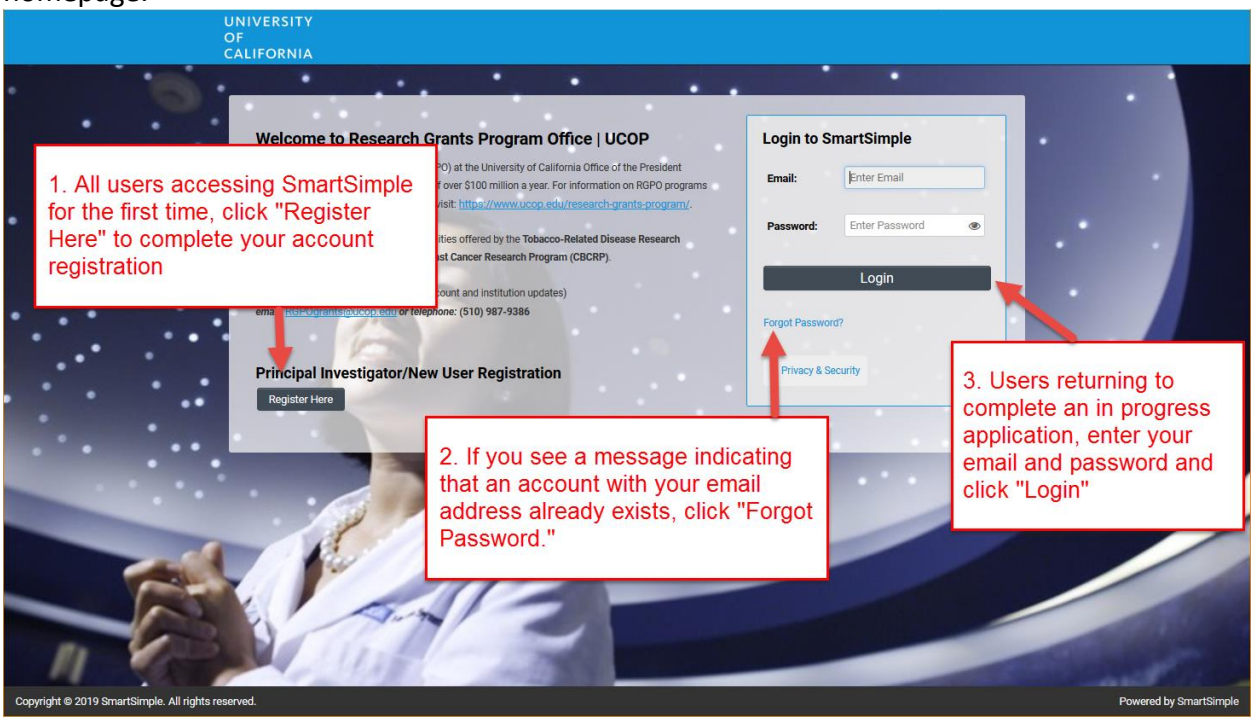
Accessing SmartSimple: https://ucop.smartsimple.com/

The Applicant must be the Principal Investigator (Applicant) of the proposal and must access SmartSimple to initiate the application process.

All Users Accessing SmartSimple for the First Time:

1. When accessing SmartSimple for the first time, all users should click the **"Register Here"** button under **"Principal Investigator Registration"** and follow the instructions to enter your institution, name, and contact information.
2. If you cannot find your institution, click **"Search the IRS database"** link. If your institution is listed in the IRS database, click the **"Select"** button (right arrow) to add it to the system and continue to #4. If it is not listed, please contact us to have your institution added to the system. Contact information can be found at the end of this document.
3. If you need to change the institution that your account is associated with, please contact us.
4. Your user account will be created. You will receive an email with instructions to create a password and complete your account profile.
5. If you see a pop-up message indicating that an account with your email address already exists, return to the main login page (https://ucop.smartsimple.com), and click the **"Forgot Password"** link. You will receive an email with a link and instructions to reset your password. **If you do not receive the password reset email within one hour, please contact us using the contact information at the end of this document. Make sure to check your spam or junk folder.**

Returning Users: Applicants who have previously registered with SmartSimple enter their username and password under **"Login"** and click the "**Login"** button on the SmartSimple homepage.



Online Proposal Submission

The proposal must be submitted using the online system SmartSimple, which can be accessed at https://ucop.smartsimple.com. **The application submission must be completed (not merely initiated) by the 12:00 noon Pacific Time deadline by using the online system SmartSimple.** Please note that SmartSimple displays all timestamps and deadlines in military time in the Pacific Time Zone. Watches and clocks on computers and office telephones are often not correct. Please plan ahead in preparing your submission, and allow a minimum of one hour to receive confirmation of your successful submission by the deadline.

Electronic Submission to Signing Official. Once all of the online data forms are completed and all of the required proposal templates and documents are completed and uploaded, the proposal is ready for electronic submission to your institution's signing official. Click the **"Submit to Signing Official"** button. This will generate an email notification to your signing official to log in, review the application, and submit or send back to you for further revision. **Note: The signing official must submit the application prior to the application deadline. Please plan submission timelines accordingly.**

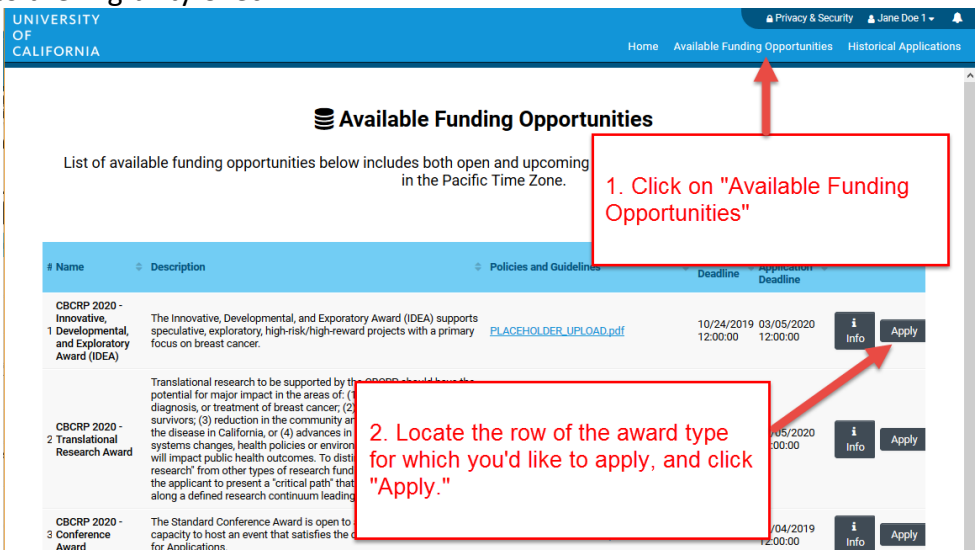
After the proposal is submitted by the signing official, an automatic email confirming the electronic submission of the proposal will be sent to the applicant and the signing official.

You may generate a PDF copy of the full proposal at any time by clicking the "**Preview**" button that appears at the top of each section of the application.

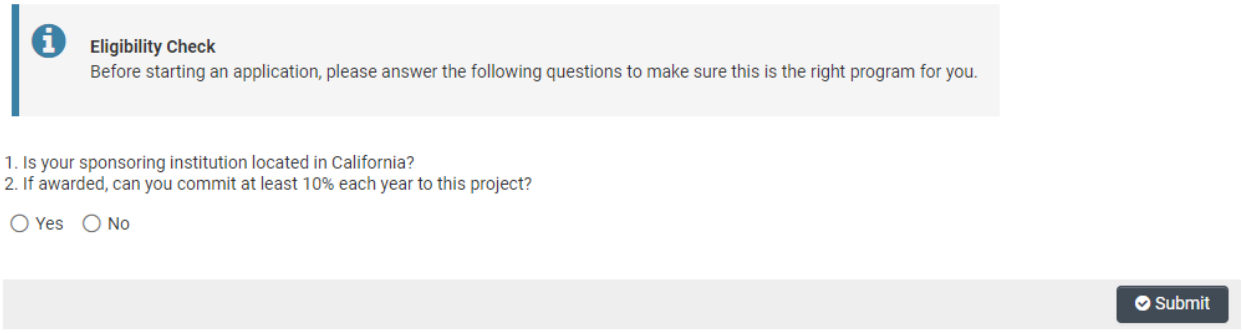
For technical assistance with SmartSimple, please contact us using the contact information provided at the end of this document.

Initiating your Hormones in Beef and Well Water Award application in SmartSimple:

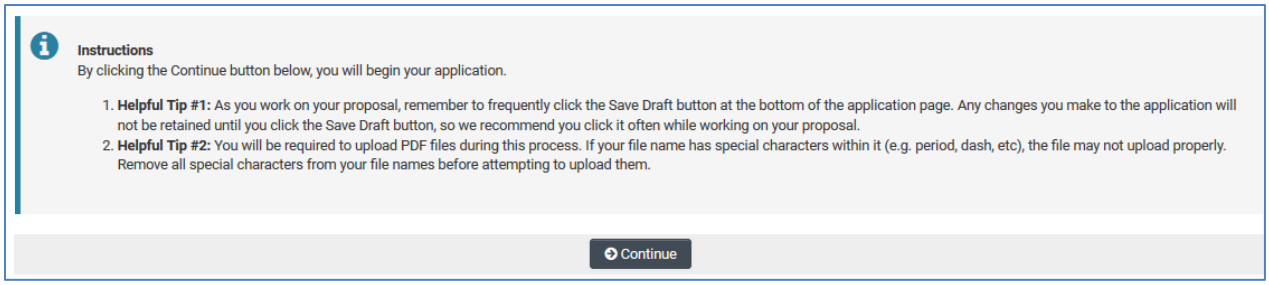
1. Once logged into the system, click on "**Available Funding Opportunities**" (upper right).
2. Find the row for the award type you are interested in, then click **"Apply."** You will then be taken to the Eligibility Check.



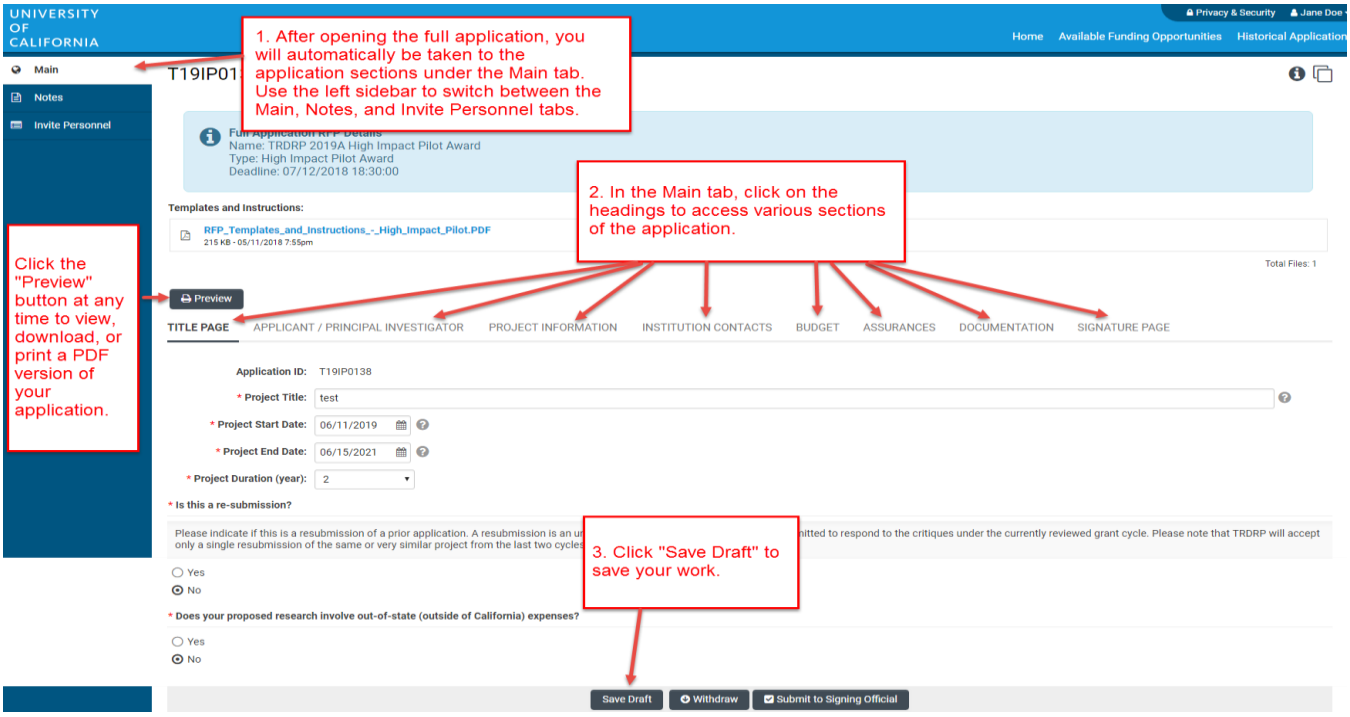
3. Complete the Eligibility Check and click **"Submit."**
    - The Eligibility Check contains a series of questions and statements regarding applicant eligibility. You must provide an answer to acknowledge that you meet all eligibility criteria mentioned. Upon submitting a "Yes" response, you will be able to start the application process. If your answer is "No," you are not eligible to apply.



4. Review the Helpful Tips, and click **"Continue"** to begin your application.

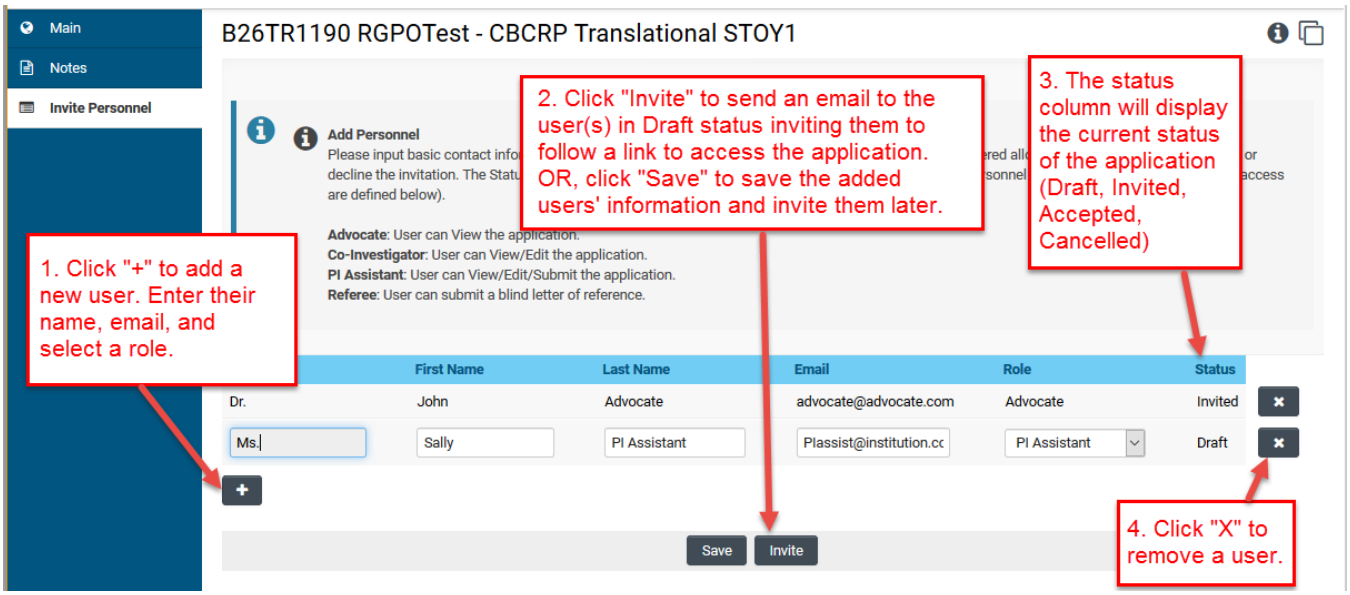


5. Once in the application interface, you will see two options on the left sidebar: Main and Notes.
    - **Main**: Click this tab to access each section of the application. Detailed instructions for each section are provided below.
    - **Notes**: Click this tab to create Notes for your application. Click "+" to add a new Note. Any Notes stored here are for the applicant's reference only and will not be reviewed by RGPO staff or reviewers. Please make sure to include all relevant project information in the application sections under the Main tab.



In addition to the Main and Notes tabs on the left sidebar, you will see the **Invite Personnel** tab.

- **Invite Personnel**: This section enables you to provide access to anyone whom you wish to participate in your application preparation or submission. Hormones in Beef and Well Water applications must add a user in the role of Advocate. Adding any additional users to this section other than the required Advocate is optional.
    1. To add a new user, click **"+"** and enter their name and email, and select a role.
        - **Advocate:** User can View the application.
        - **Co-Investigator:** User can View the application.
        - **PI Assistant:** User can View/Edit/Submit the application.
        - **Referee:** User can submit a blind letter of reference at the full application stage for specific application types. CBCRP applicants should not use this role.
    2. Once you have added a user, click **"Save"** to save the user's information, and/or click **"Invite"** to send an invitation email to the user. The invitee will receive an email invitation from the system with instructions to access the application.
    3. Add additional users by clicking **"+"** and entering the users' information, repeating for all users. Once you have added all desired users, click **"Save"** to save the information in batch, or **"Invite"** to invite all users in batch. The Status column will display the current status of the invitation. Click the "**X**" button on the far right to remove a user.



Application Sections

The following instructions correspond to the sequence of Proposal Sections that appear horizontally from left to right in the application in SmartSimple. The application sections: **Title Page, Applicant/Principal Investigator, Project Information, Institution Contacts, Budget, Assurances, Documentation, and Signature Page,** can be completed in any order and in any number of sessions prior to the deadline. You can move between sections by clicking directly on the section headings. Required fields are denoted with a red asterisk (*). Please be sure to save your work after each entry.

Complete the online data forms in SmartSimple as described below. Please be sure to **save your work after each entry**. To avoid loss of data, we recommend that you save your work every 10 to 15 minutes. For security reasons, if your session is idle (i.e. if you don't press **"Save"** or click on a link to move to another page) for an extended period of time, you will be automatically logged off and any unsaved data will be lost.

Note about record being locked: The application can be accessed by one user at a time. If you are unable to edit your application, it is likely in use by another user. A message will appear at the bottom of the screen indicating that the application is currently locked. You will not be able to access the application until the first user closes their session.

Application Section 1: Title Page

- **Project Title:** Enter a title that describes the project in lay-friendly language. (Max 100 characters)
- **Project Duration:** Enter a project duration for up to two years.
- **Proposed Project Start Date:** Enter a project start date of June 1, 2020

- **Proposed Project End Date:** Enter a project end date of May 31, 2021 for a one year award or May 31, 2022 for a two year award.

Application Section 2: Applicant/Principal Investigator

Applicant/Principal Investigator information will be auto-populated from the "My Profile" section of your SmartSimple account. Please review this information for accuracy. To make changes to this information, click on your name in the upper right corner of the page, and select **"My Profile."** Update your information and save your changes. Return to the full application by selecting **"Open"** under **"In Progress Applications"** on the Home screen. You can also go directly to the "My Profile" page in your account to make changes at any time.

- Please note that not all information on the Applicant/PI profile is required.
- A required field entitled "ORCID ID" is editable on the Professional Profile Page. 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 obtain an ORCID 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.

Application Section 3: Project Information

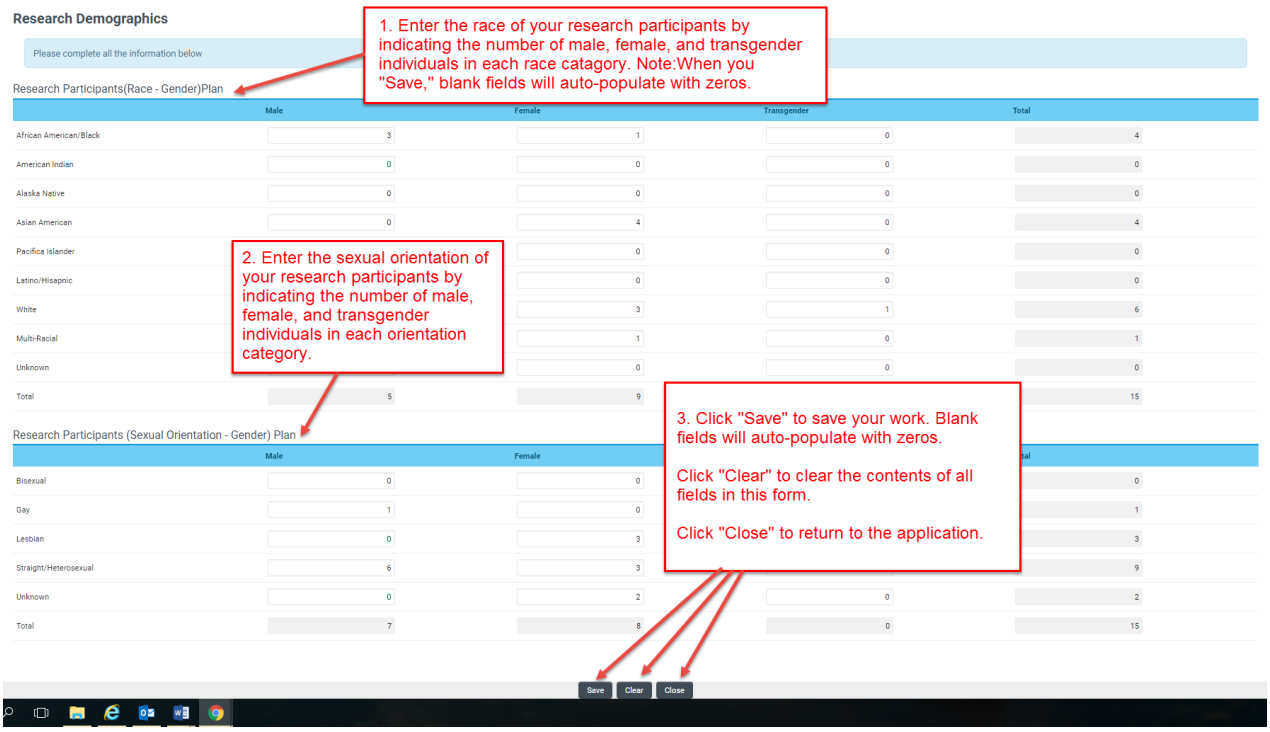
- **Lay Abstract:** Provide a concise summary of your project in non-scientific terms that would be understood by a lay audience, evaluated mainly in the programmatic review. The abstract should be written using a style and language comprehensible to the general public. Avoid the use of acronyms and 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. Include the following elements:
  - 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 description should be no more than 2400 characters in length (approximately 350 words) to avoid truncation. Please check the entry after saving to be sure you have not exceeded the character limitations.
- **Scientific Abstract:** Provide a concise summary of your project in technical terms that would be appropriate for experts in the field, evaluated mainly in the peer review. 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. Include the following elements:

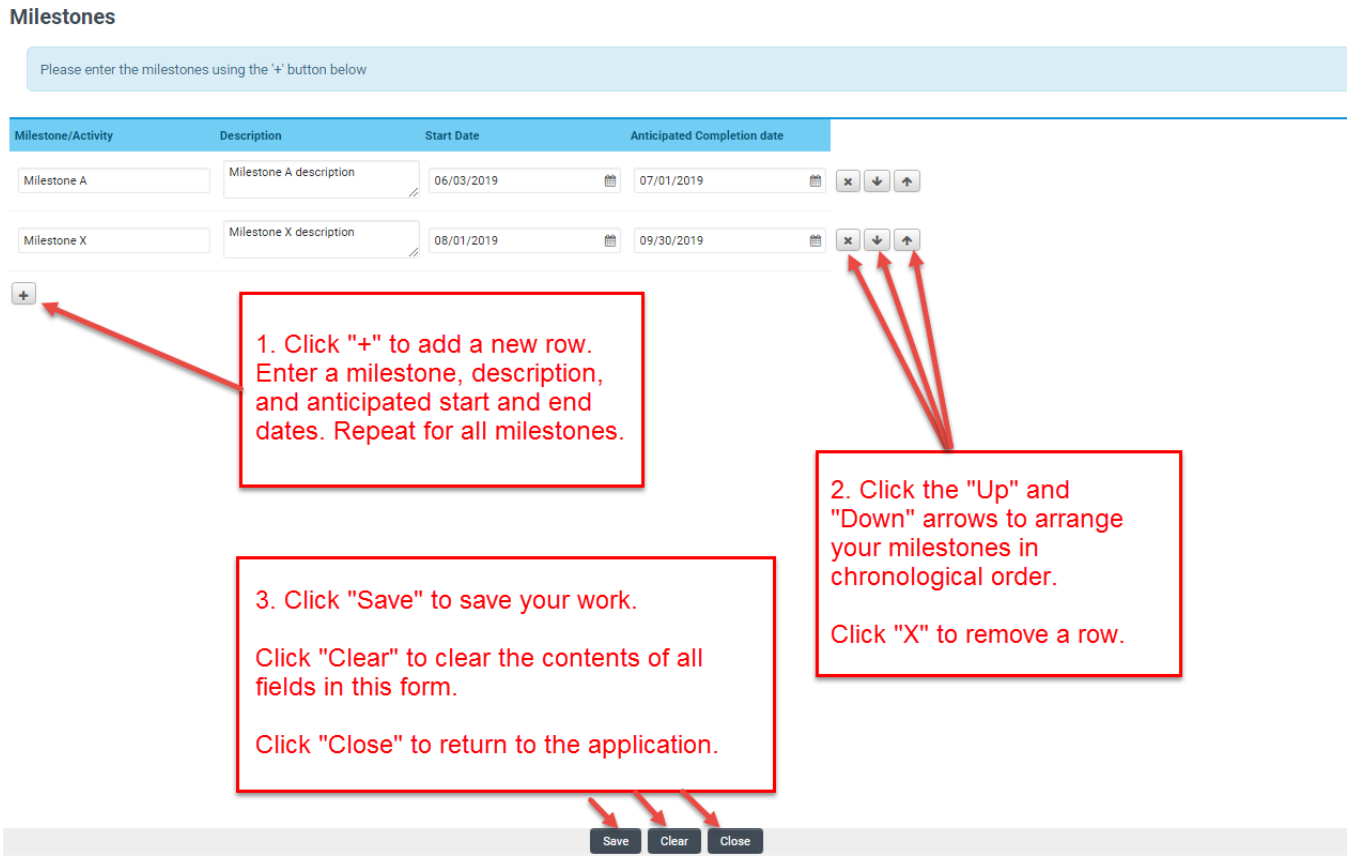
- A short introductory paragraph indicating the background and overall topic(s) addressed by the research project
- The central hypothesis or questions to be addressed in the project.
- A listing of the objectives or specific aims in the research plan
- The major research methods and approaches used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

The description should be no more than 2400 characters in length (approximately 350 words) to avoid truncation. Please check the entry after saving to be sure you have not exceeded the character limitations.

- **Specific Aims:** Describe the specific aims of your project (2400 character maximum).
- **Keywords:** Please provide a **minimum of three and up to five** keywords that best reflect your research to optimize peer review selection in the each of the keywords textboxes provided. Please use words not in the title. (Each set of keyword(s) should be 25 characters or less)
- **Research Priority:** All applications must address one or more of CBCRP's four research priorities. **Applicants to the Hormones in Beef and Well Water initiative should select the Etiology and Prevention category using the drop-down list:**
    1. *The Community Impact of Breast Cancer*
    2. *Etiology and Prevention*
    3. *Biology of the Breast Cell*
    4. *Detection, Prognosis and Treatment*
- **CSO Research Type(s) and Sub-Type(s):** Please select the CSO Type(s) and corresponding Sub-Type(s) that best represent your project. 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.
- **Subject Area(s):** Select the subject area(s).
- **Focus Area(s):** Start typing your project's focus area and the system will populate options. Please see Appendix B for a full list of available focus areas.
- **Research Demographics:** Complete this table if the research project will involve human subjects. Enter the target demographics of the research participants that you propose to recruit. Click **"Enter Research Demographics."** A separate window will open. Enter numerical digits in the applicable fields to indicate the race and sexual orientation of your research participants, organized by gender. Totals will calculate at the end of each demographic section. Click **"Save"** to save your changes. Click **"Close"** to return to the full application. A summary of the research demographics that you entered will populate.


Research Demographics
Please complete all the information below
1. Enter the race of your research participants by indicating the number of male, female, and transgender individuals in each race catagory. Note:When you "Save," blank fields will auto-populate with zeros.
Research Participants(Race - Gender)Plan
Male
Female
Transgender
Total
African American/Black 3 1 0 4
American Indian 0 0 0 0
Alaska Native 0 0 0 0
Asian American 0 4 0 4
Pacifica Islander 0 0 0
Latino/Hisapnic 0 0 0
White 3 1 6
Multi-Racial 1 0 1
Unknown 0 0 0
Total 5 9 15
2. Enter the sexual orientation of your research participants by indicating the number of male, female, and transgender individuals in each orientation category.
Research Participants (Sexual Orientation - Gender) Plan
Male
Female
Bisexual 0 0 0
Gay 1 0 1
Lesbian 0 3 3
Straight/Heterosexual 6 3 9
Unknown 0 2 0 2
Total 7 8 0 15
3. Click "Save" to save your work. Blank fields will auto-populate with zeros.
Click "Clear" to clear the contents of all fields in this form.
Click "Close" to return to the application.
Save
Clear
Close

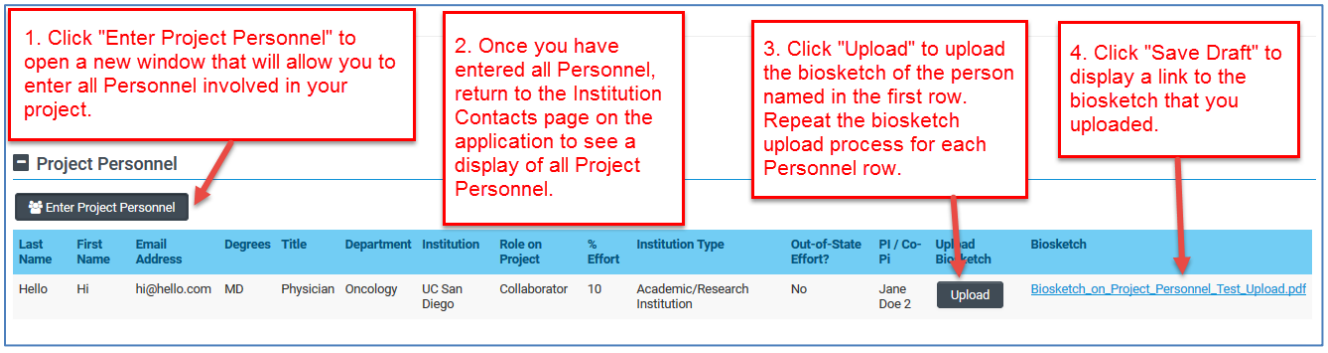
- **<u>Milestones and Timetable</u>:** Add significant milestones that are described in your research plan to this table along with anticipated completion dates and arrange them in chronological order. Click **"Enter Milestones."** A separate window will open. Click **"+"** to add a row and enter a milestone. Repeat for additional milestones. Use the **"Up"** and **"Down"** arrows at the right of each row to arrange your milestones in chronological order. Click **"X"** to remove a row. Click **"Save"** to save your changes. Click **"Close"** to return to the full application. A summary of the milestones that you entered will populate.



Application Section 4: Project Contacts

- **<u>Institution Contacts</u>:** This is a read-only display of the Institution Contacts you enter on the Budget tab. You do not need to enter any institution contacts here.

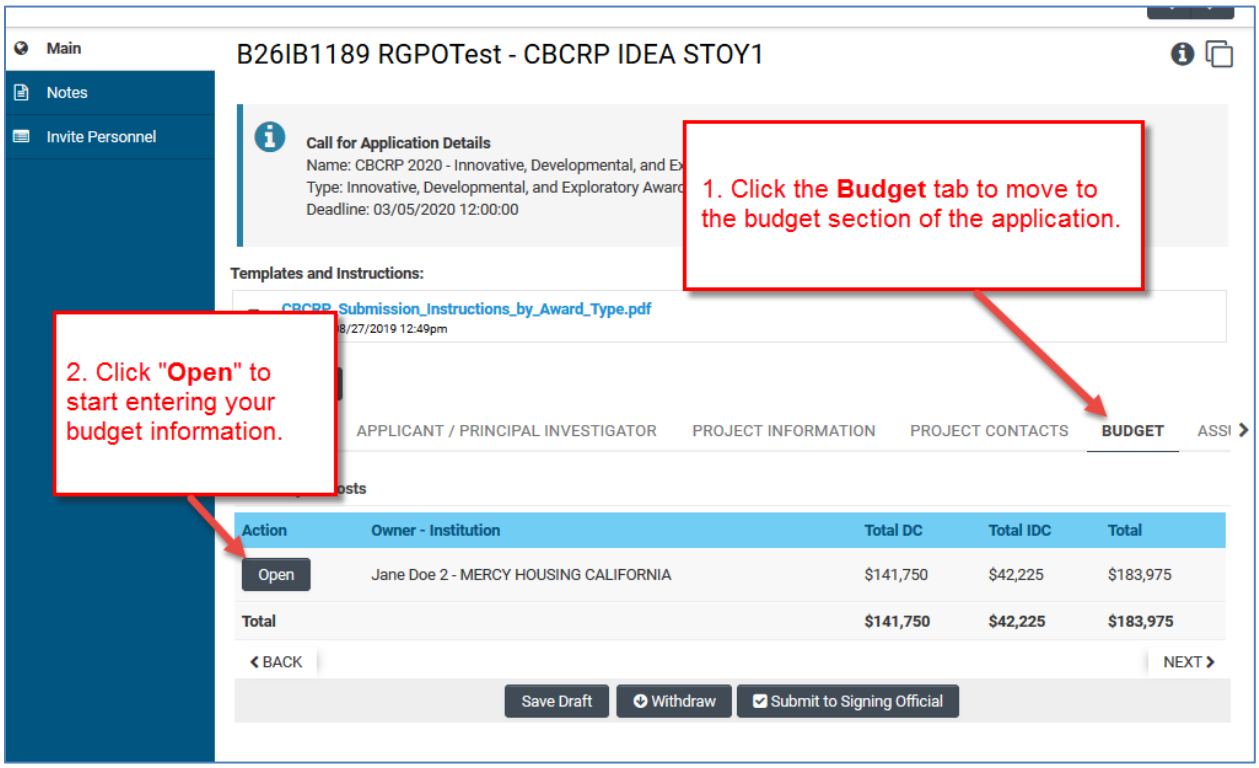
- **<u>Project Personnel</u>:** You **MUST** add all project personnel as specified in Appendix C. Click **"Enter Project Personnel."** A separate window will open. Using the **"+"** button, enter the names and details of all project personnel. Add rows until you have added all project personnel. Click **"Save"** to save your changes. Click **"Close"** to return to the full application. Please see Appendix C for Project Personnel definitions and guidelines.
    - **<u>Out-of-State Effort</u>**: Please indicate (Yes/No) if your proposed research involves Out-of-State (outside of California) expenses.
    - **<u>PI/Co-PI</u>**: Please select the Principal Investigator on the project from the drop down menu
    - **<u>Upload Personnel Biosketches</u>**: Once you close the Project Personnel window and return to Project Contacts tab, you will see a display of your Personnel. Click the **Upload** button to upload the biosketch of the person named in the first row, and the biosketch upload process for each Personnel listed. Then click "**Save Draft**" to display a link to the biosketch that you uploaded.



Application Section 5: Budget

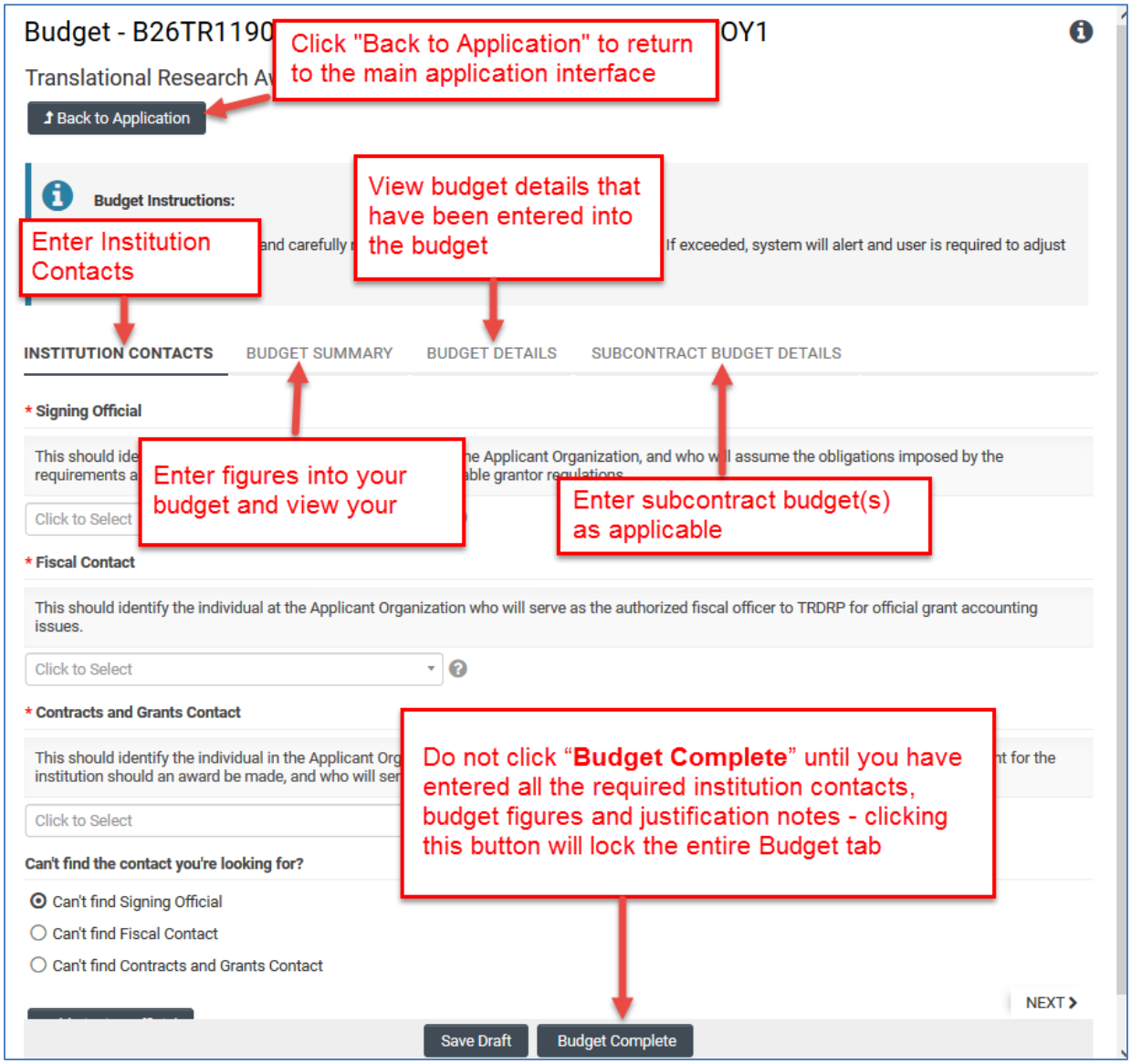
This section contains five sub-tabs: Institution Contacts, Budget Summary, Budget Details, Subcontract Budget Details, and Project Contributions. Complete the information in the Institutional Contacts, Budget Summary, Budget Detail and, if applicable, Subcontract Budget Details tab as described in instructions below. Do not complete the Project Contributions tab.

Click "**Open**" to begin this section.



Do not click "Budget Complete" until you have entered all the required institution contacts, budget figures and justification notes – clicking this button will lock the entire Budget tab and you will not be able to make additional edits. Do not click "Budget Complete" until you are ready to submit your application to your signing official.

This section contains four sub-tabs: **Institution Contacts, Budget Summary, Budget Details, and Subcontract Budget Details**



- **<u>Institution Contacts</u>:** Three contact types are required for every application:

    - **Signing Official:** This should identify the individual who is authorized to act for the Applicant Organization, and who will assume the obligations imposed by the requirements and conditions for any grant, including the applicable the grantor's regulations.
        - When all online forms and downloaded templates have been completed and uploaded to SmartSimple, the application will be ready to be electronically submitted to your institution's signing official.

- **Your institution's signing official will receive an email notification to log in, review, and electronically submit the application. Note: The signing official must complete this step prior to the application deadline. Please plan submission timelines accordingly.**

- **Contracts and Grants Official:** This should identify the individual in the Applicant Organization's Contracts and Grants Office, or comparable unit, who will administer the grant for the institution should an award be made, and who will serve as the liaison to the grantor on official grant administrative issues.

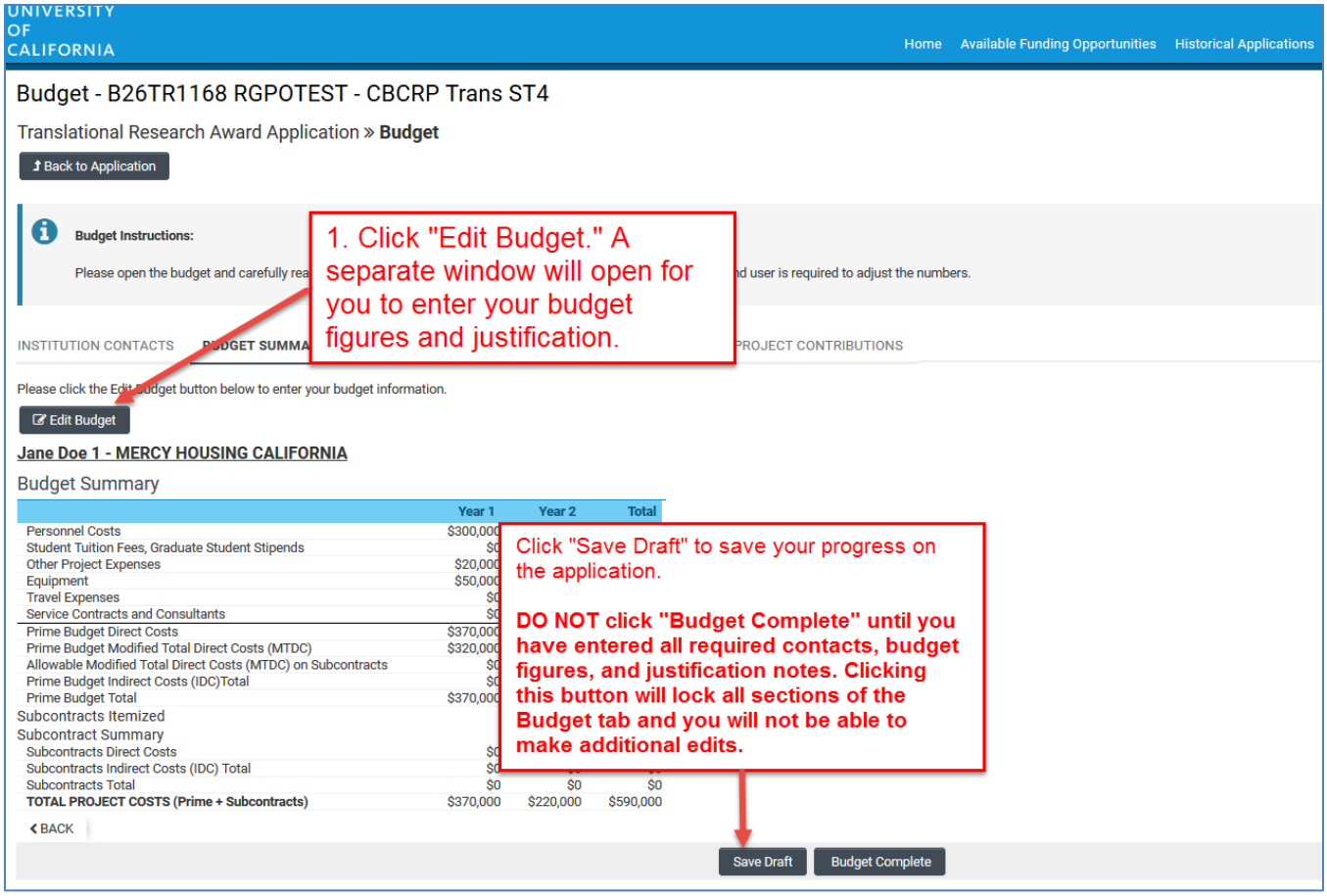
- **Fiscal Contact:** This should identify the individual at the Applicant Organization who will serve as the authorized fiscal officer to the grantor for official grant accounting issues.

To add these individuals as contacts of your application, start typing the official's name in the appropriate field and select a contact that populates. If you cannot find the contact name in the populated list, answer the question "Can't find the contact you're looking for?" If applicable, click the radio button next to **"Can't find Signing Official."** Then click **"Add Signing Official."** A pop-up window will open where you can enter the signing official's full name and email. The contact's name should now appear in the drop down menu of the role to which the contact was added. Repeat this process to add a Fiscal Contact and Contracts and Grants Contact as necessary. **Do not use generic emails such as "ContractsandGrants@myinstitution.edu."**

- **<u>Budget Summary</u>**

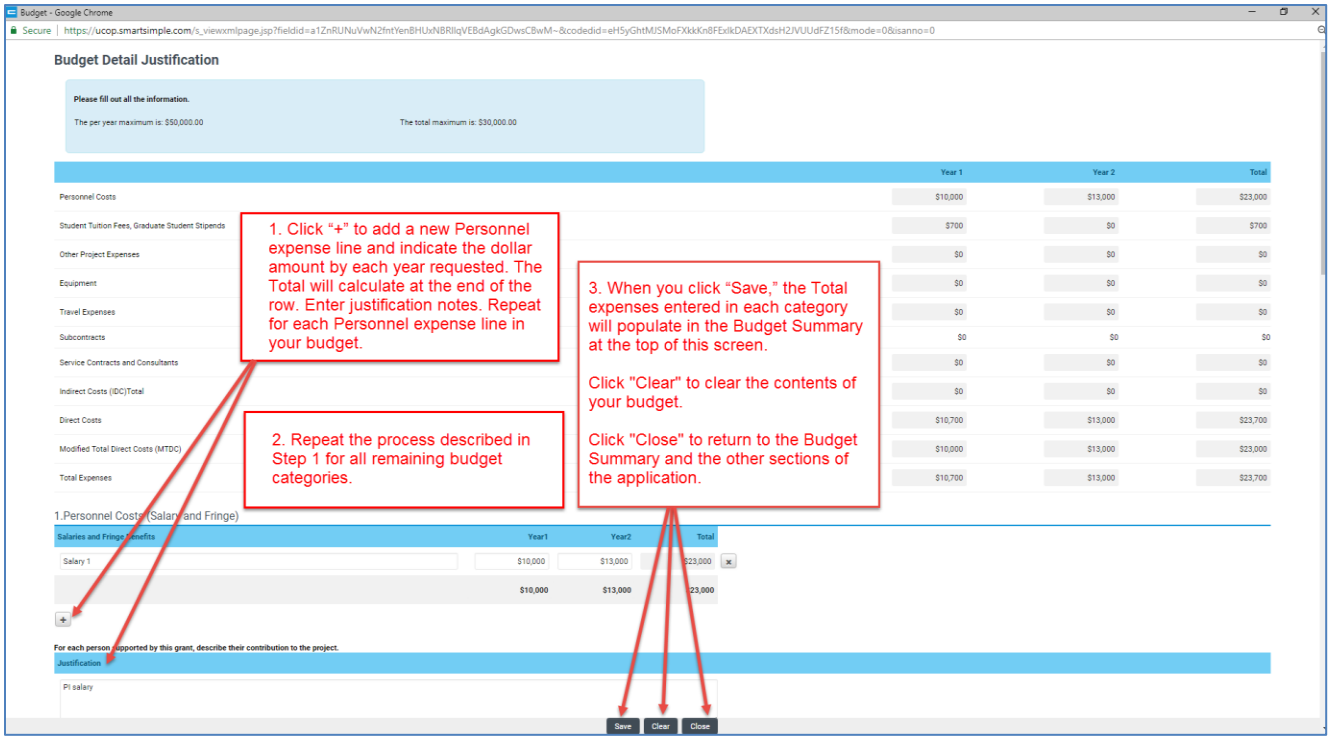
1. To complete your application budget, go to the "Budget Summary" tab within the main Budget tab. A complete detailed budget must be submitted with a full application. Subcontractor budgets can be created as required. Click **"Save Draft"** to save your progress on the application before entering the budget information. Refer to Appendix D for Cost and Expense Guidelines.

2. Under the Budget Summary heading, click **"Edit Budget."** A separate window will open.

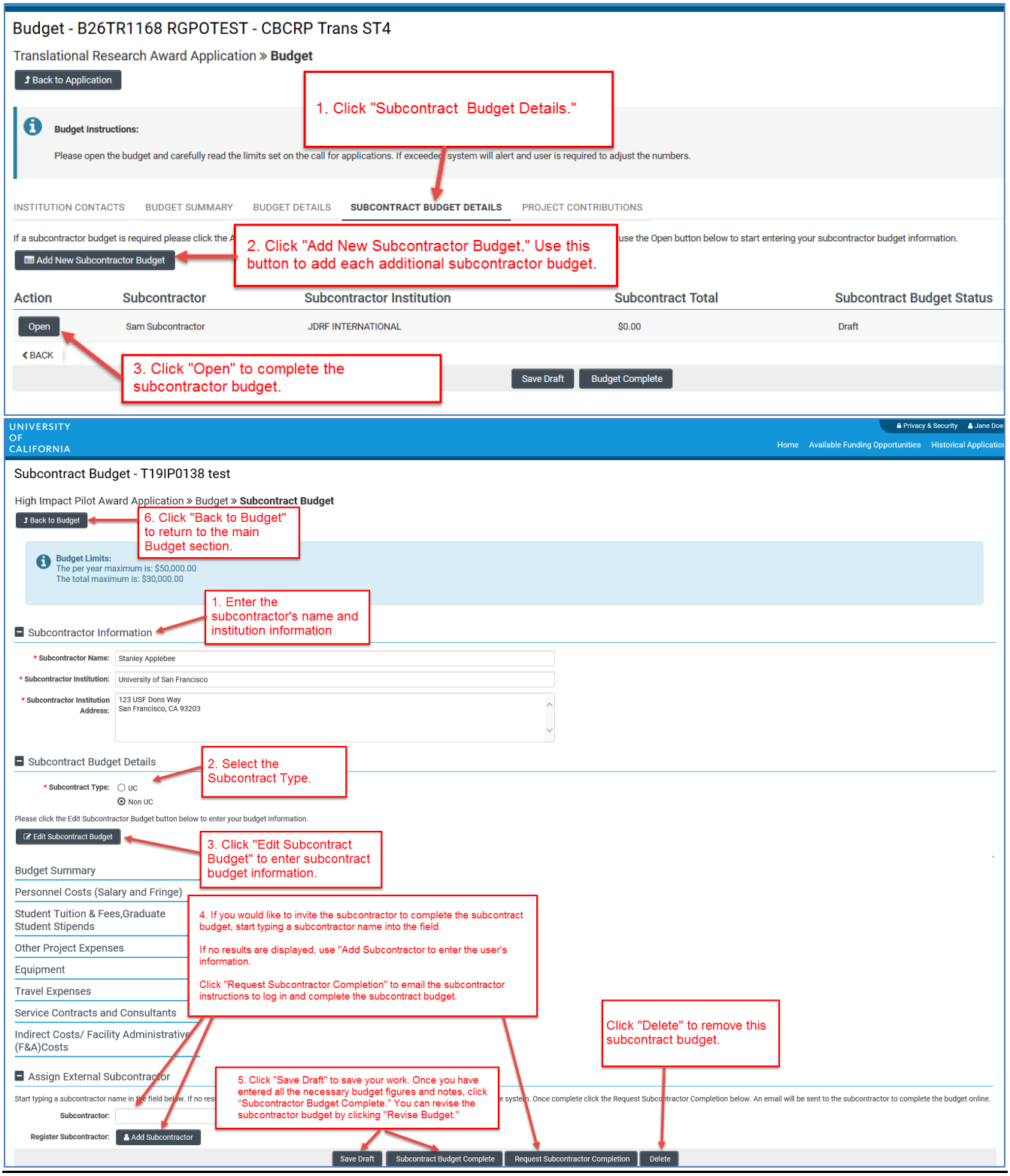


3. Scroll down to **1. Personnel Costs (Salary and Fringe)**. Click **"+"** to add a new Personnel expense and indicate the dollar amount by each year requested. The Total will calculate at the end of the row. Enter justification notes. When you click **"Save,"** the expense will populate in the Budget Summary at the top of this screen. Repeat this step for each Personnel expense in your budget. **The minimum "Months Devoted to Project" required for the PI is 1.2 months (= 10% FTE).**

4. Repeat this process for each of the remaining budget categories, as applicable. Please refer to Appendix D for Cost and Expense Guidelines for all applications.
   - **Student Tuition Fees, Graduate Student Stipends**
   - **Other Project Expenses**
   - **Equipment**
   - **Travel Expenses**
   - **Service Contracts and Consultants**
   - **Indirect Costs/Facility Administrative (FA) Costs**
     - Please note you must manually calculate and enter the Indirect Costs based on your Modified Total Direct Costs (MTDC). Refer to Appendix D for details on indirect costs.



- **<u>Budget Justification</u>:**
  - A textbox is available under each budget category to provide the budget justification relevant to that particular category. There is no character limit on the budget justification, though the expectation is that the justification is concise.
- **<u>Subcontractor Budget(s)</u>:**
  - A separate budget must be provided per subcontract. If applicable, click the **"Subcontract Budget Details"** heading, then **"Add New Subcontractor Budget,"** then **"Open"** to enter subcontract budget information.
  - Enter the subcontractor's name and institution information. Click **"Edit Subcontract Budget"** to complete the subcontract budget using the same instructions you used to complete the application's project budget (listed above).
  - If you would like to invite the subcontractor to complete the subcontract budget, scroll to "Assign External Subcontractor" and start typing a subcontractor name into the Subcontractor field. If no results are displayed, click **"Add Subcontractor"** to enter the user's information. Click **"Request Subcontractor Completion"** to email the subcontractor instructions to log in and complete the subcontract budget.
  - Once you have entered all the necessary budget figures and notes, click **"Subcontractor Budget Complete."** You can revise the subcontractor budget by clicking **"Revise Budget."**
  - Click **"Back to Budget"** to return the application's project budget.


Budget - B26TR1168 RGPOTEST - CBCRP Trans ST4
Translational Research Award Application » Budget
Back to Application
1. Click "Subcontract Budget Details."
Budget Instructions:
Please open the budget and carefully read the limits set on the call for applications. If exceeded system will alert and user is required to adjust the numbers.
INSTITUTION CONTACTS
BUDGET SUMMARY
BUDGET DETAILS
SUBCONTRACT BUDGET DETAILS
PROJECT CONTRIBUTIONS
2. Click "Add New Subcontractor Budget." Use this button to add each additional subcontractor budget.
Add New Subcontractor Budget
Action
Subcontractor
Subcontractor Institution
Subcontract Total
Subcontract Budget Status
Open
Sam Subcontractor
JDRF INTERNATIONAL
$0.00
Draft
BACK
3. Click "Open" to complete the subcontractor budget.
Save Draft
Budget Complete
UNIVERSITY OF CALIFORNIA
Privacy & Security
Jane Doe
Home
Available Funding Opportunities
Subcontract Budget - T19IP0138 test
High Impact Pilot Award Application » Budget » Subcontract Budget
Back to Budget
6. Click "Back to Budget" to return to the main Budget section.
Budget Limits:
The per year maximum is: $50,000.00
The total maximum is: $30,000.00
1. Enter the subcontractor's name and institution information
Subcontractor Information
Subcontractor Name:
Stanley Applebee
Subcontractor Institution:
University of San Francisco
Subcontractor Institution Address:
123 USF Dons Way
San Francisco, CA 93203
Subcontract Budget Details
2. Select the Subcontract Type.
Subcontract Type:
UC
Non UC
Please click the Edit Subcontractor Budget button below to enter your budget information.
Edit Subcontract Budget
3. Click "Edit Subcontract Budget" to enter subcontract budget information.
Budget Summary
Personnel Costs (Salary and Fringe)
Student Tuition & Fees,Graduate Student Stipends
Other Project Expenses
Equipment
Travel Expenses
Service Contracts and Consultants
Indirect Costs/ Facility Administrative (F&A)Costs
4. If you would like to invite the subcontractor to complete the subcontract budget, start typing a subcontractor name into the field.
If no results are displayed, use "Add Subcontractor to enter the user's information.
Click "Request Subcontractor Completion" to email the subcontractor instructions to log in and complete the subcontract budget.
Click "Delete" to remove this subcontract budget.
Assign External Subcontractor
Subcontractor:
Register Subcontractor:
Add Subcontractor
5. Click "Save Draft" to save your work. Once you have entered all the necessary budget figures and notes, click "Subcontractor Budget Complete." You can revise the subcontractor budget by clicking "Revise Budget."
Save Draft
Subcontract Budget Complete
Request Subcontractor Completion
Delete

- **<u>Project Contributions</u>: CBCRP applicants should ignore this section.**
- **<u>Overall Budget Completion</u>:**
    - When you have finished filling out your entire budget, click **"Save,"** then **"Close."**
    - You can easily view the budget figures you entered by clicking the "**Budget Summary"** and "**Budget Details"** headings. Click **"Edit Budget"** to make updates or changes to these budget sections.
    - If you would like to work on other sections of the application and return to the Budget later, click **"Save Draft,"** then **"Back to Application."**
    - Once you have entered all the necessary institution contacts, budget figures, and notes, click **"Budget Complete." Note: Clicking "Budget Complete" will lock the entire Budget section and you will not be able to make additional edits.**

Application Section 6: Organization Assurances
Answer the Yes/No questions regarding the usage of vertebrate animals, human subjects, biohazards, and DEA substances.

If you answered "Yes" to any of the questions, indicate the assurance status for each type of usage:

- Under Animal Use, click **"Enter IACUC Details."** A new window will open.
    - Click **"+"** to add a new row.
    - As applicable, enter the approval and expiration dates, and assurance number. Click **"Save,"** then **"Close."**
    - Click **"Upload"** to upload assurance documentation.
    - Repeat for all Animal Use assurances.
- Repeat the steps above for Human Subjects (click **"Enter IRB Details"**), Biohazard (click **"Enter Biohazard Details"**), and DEA Controlled Substance (click **"Enter DEA Substance Details"**), as applicable. Some responses may prompt additional questions that you should complete.

Application Section 7: Documentation: Proposal Templates
Appendix A contains a list of documentations/templates and their requirements. Additional instructions and guidance are located on top of each template. All required items to complete and upload are listed. All uploads must be in PDF format. Listed below are the forms and templates you download from SmartSimple, enter text, convert to PDF, and, unless instructed otherwise, re-upload to your application in this section.

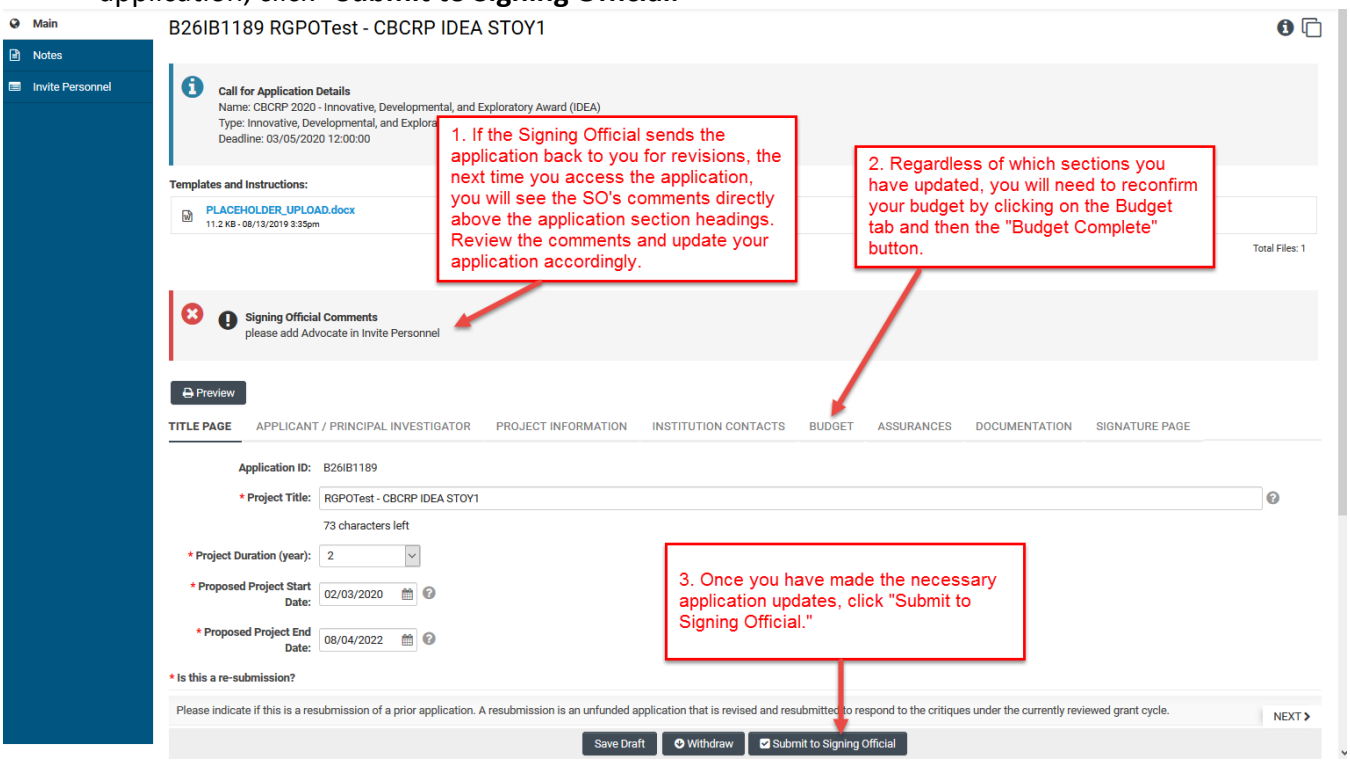
Note: *Please make sure that your uploaded PDFs are not password protected and do not contain electronic signatures.*

Application Section 8: Signature Page

Once all online and downloaded templates have been completed and uploaded to SmartSimple, the application is ready to be submitted to your institution's signing official. You must click **"Submit to Signing Official"** to complete this step.

Your institution's signing official will receive an email notification to log in, review, and either submit the application, or send the application back to the Applicant PI for revision. **Note: The signing official must complete this step prior to the application deadline. Please plan submission timelines accordingly.**

- If the signing official's submission was successful, a confirmation message will appear on the screen and a confirmation email will be sent to the Applicant PI. The email confirmation typically arrives within a few minutes (the length of time may be greater near the submission deadline). If you do not receive the SmartSimple confirmation email within an hour of your submission, please contact us using the contact information at the end of this document. You can also confirm the status of your application submission by going to the Home screen, and clicking on **"Submitted/Under Review Applications."**
- If the signing official sends the application back to you for further revision, you will receive an email notification. When you next log in and open your application, you will see any comments made by the signing official at the top of the application interface. Update the application as needed. **Note:** Regardless of which sections you have updated, you will need to reconfirm your budget by clicking on the Budget section and then **"Budget Complete."** Once you have made the necessary updates to your application, click **"Submit to Signing Official."**



Appendix A: CBCRP 2020 Cycle 26 Proposal Form Upload Requirements

Upload (form) item	Page limit	Required or optional
Research Plan	**12 + 3 (references)**	**Required**
Program Responsiveness	**2**	**Required**
Facilities	**1 per institution**	**Required**
PI Biographical Sketch & Other Support (use NIH Biosketch)	**5 (each biosketch)**	**Required**
Advocacy Involvement	**1**	**Required**
Letter of Commitment	**No limit**	**Required**
Human Subjects	**No limit**	**Required (with or without human subject involvement)**
Vertebrate Animals	**No limit**	**Optional**
Appendix List and uploads	**30**	**Optional**

Detailed Description of Proposal Templates:

Research Plan (REQUIRED)

This section is the **most important** for the peer review. Note carefully the page limits, format requirements, and suggested format. **Limit the text to twelve pages, with an additional 3 pages 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.

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.

Program Responsiveness (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.

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.

Facilities (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 (version 2015 or later) for each key person and attached in the Project Personnel section. Limit the length of each biosketch to *no more than* five (5) pages**.

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**.

Human Subjects (REQUIRED)

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 Assurances tab, 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.

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 CBCRP as soon as possible, but no later than June 1, 2020. Funds will not be released until all assurances are received by 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 may be included.

Appendix B: Focus Areas

Animal Sciences	Electronics and Electronics Manufacturing	Nanotechnology
Anthropology	Energy	Networking and Internet Technologies
Art and Art Practice	Energy Policy	Neuroscience
Astronomy and Astrophysics	Engineering	New Nicotine Products
Atmospheric Science	Engineering – Chemical	Nicotine Dependence
Behavioral Sciences	Engineering – Civil	Nuclear Sciences
Biochemistry	Engineering – Electrical	Opportunistic Infections
Bioengineering and Biotechnology	Engineering – Mechanical	Pathogenesis
Biofuels	Engineering – Nuclear	Patient Safety Research
Biology	Environmental Sciences	Physics
Biology- Molecular/Cell	Epidemiology	Planetary and Space Science
Biophysics	Etiology	Plant Science
Cancer – Breast	Evaluation Research	Plasma Physics
Cancer – Lung	Gender and Women's Studies	Policy
Cancer – Other	Genomics/proteomics	Political Science
Cancer Detection Methods	Geography	Prevention
Cardiovascular Disease	Geology	Prognosis
Chemistry	Health and Wellness	Psychology
Climate Studies and Climate Change	Healthcare Services and Systems	Pulmonary Diseases
Communications	History	Race and Ethnicity
Community Engaged Research	HIV/AIDS	Security Studies
Community-based Participatory Research	Humanities	Sexuality Studies
Computer Science	Imaging	Socioeconomic Status
Cosmology	Immigration	Sociology
Criminology and Incarceration	Immunology	Solar Energy
Cultural Studies	Information Technology	Statistics
Demography	International and Area Studies	Stem Cell Biology
Developmental Biology	Interventions	Theoretical Physics
Digital Media	Languages and Linguistics	Therapeutics/Treatment
Disease Transmission	Marine and Oceanic Sciences	Tobacco Use
Disparities and Social Inequality	Materials Science and New Materials	Tobacco Use Cessation
Earth Science and Geophysics	Mathematics and Computational Sciences	Toxicology
Economics	Microelectronics	Vaccine Development
Education	Molecular Biology	

Appendix C: Project Personnel Roles – Definitions, Guidelines, and Biosketch Requirements

The Research Grants Program Office uses NIH definitions for allowable roles in the project personnel:

- **Applicant Principal Investigator:** The Principal Investigator (PI) serves as the proposal applicant, and is the recipient of the award. He/she serves as the project's main research and administrative contact, and is responsible for providing progress, fiscal and other reports to the Program office. See the call for applications for eligibility requirements.
    - Note: for the majority of our award types, there is only one applicant who serves at the PI; there is no such role as Co-Principal Investigator or Co-PI. Refer to the program's call for applications for exceptions.
    - A **Biographical Sketch** must be provided for the Applicant Principal Investigator.
    - University of California Investigators who do not have PI status at the University must submit evidence of a waiver of UC PI status in the Appendix. This does not apply to fellowships.

- ***Co-Principal Investigator:*** ***For partnered award types which allow multiple PIs,*** *Co-Principal Investigators (Co-PIs) serve as a second proposal applicant, and is the recipient of a separate award for the proposed project. He/she serves as the main research and administrative contact for his/her institution, and is responsible for providing progress, fiscal and other reports to the Program office. See the call for applications for eligibility requirements.*
    - *Refer to the program's call for applications for the description of partnered mechanisms which allow a co-Principal Investigator or Co-PI.*
    - *A* ***Biographical Sketch*** *must be provided for the co-Principal Investigator.*
    - *University of California Investigators who do not have PI status at the University must submit evidence of a waiver of UC PI status in the Appendix. This does not apply to fellowships.*
    - ***This role should not be used for applications to the Hormones in Beef and Well Water RFP.***

- **Co-Investigator(s):** Co-investigators (Co-Is) are defined as individuals with independent responsibility for the design, conduct and reporting of research, whether or not their salaries are included in the Budget request. Typically, these individuals have doctoral or other professional degrees, although individuals with master's or baccalaureate degrees should be included if their involvement meets the definition of co-investigator.
    - A **Biographical Sketch** must be provided for each co-investigator listed.
    - A Co-Investigator as part of a subcontract from a University of California campus must have UC PI status.
        - University of California Investigators who do not have PI status at the University must submit evidence of a waiver of UC PI status in the Appendix.

- **Trainee(s)** are defined as undergraduate students, graduate students, and most postdoctoral researchers who do not meet the definition of Principal Investigator or Co-Investigator. Use "TBN-1, TBN-2…" for trainees or staff to be hired at a later date.
    - Do not provide Biographical Sketch for trainees.

- ***Dissertation Advisor(s)*** *are senior investigator(s) responsible for guiding the applicant's dissertation research. This role serves as the mentor for the predoctoral fellowship applicant.*
    - *Predoctoral Fellowship requires at least one dissertation advisor, and may have limited or no other project personnel involved.*
    - *The dissertation advisor must provide a blinded letter of recommendation through the* ***Letters of Recommendation*** *section on SmartSimple. Refer to the application instructions for additional details.*
    - *A* ***Biographical Sketch*** *must be provided for the dissertation advisor.*
    - *A percentage % effort is not required from the dissertation advisor.*
    - ***This role should not be used for applications to the Hormones in Beef and Well Water RFP.***

- ***Research Advisor(s)*** *are senior investigator(s) responsible for guiding your postdoctoral research. This role serves as the mentor for the postdoctoral fellowship applicant.*
    - *Postdoctoral Fellowship requires at least one research advisor, and may have limited other personnel involved.*
    - *The research advisor must provide a blinded letter of recommendation through the* ***Letters of Recommendation*** *section on SmartSimple. Refer to the application instructions for additional details.*
    - *A* ***Biographical Sketch*** *must be provided for the research advisor.*
    - *A percentage % effort is not required from the research advisor.*
    - ***This role should not be used for applications to the Hormones in Beef and Well Water RFP.***

- **Collaborator(s)** are project participants who are intellectually engaged in the research, yet are not the Principal Investigator or Co-Investigators, and are not members of the investigator's research or technical support staff.
    - A letter of commitment to participate from each collaborator must be included in the Appendix.
    - A **Biographical Sketch** must be provided for each collaborator listed.

- **Advocate(s)** are individuals who provide the experience and knowledge of those affected by the disease to inform the design, conduct and reporting of the research. Advocates are associated with an advocacy organization or community pertinent to the project.
    - The advocate participation in the project must be described using the **Advocacy Involvement** template and the project confirmed using the **Letter of Commitment** template.
    - All advocacy costs must be budgeted and justified in the Advocacy Expenses in the Other Project Expenses section of the budget.

- A biographical sketch may be included for the advocate.
- A percentage % effort is not required from the advocate.

- **Consultant(s)** are project participants who provide a well-defined and restricted service. Provide the names and organizational affiliations of all consultants, other than those involved in consortium/contractual arrangements. Include consultant physicians in connection with patient care and persons who serve on external monitoring boards or advisory committees to the project. Payment of a consultant's services, exclusive of expenses, may not exceed the consultant's normal rate or the daily maximum rate established by the University, whichever is less.
  - All consultant costs must be justified in the **Budget Justification**. It is expected that consultant services will be limited to those essential services that are unavailable at the prime institution, and that the costs will not constitute a significant portion of the proposal budget (generally 10-15% of direct costs or less).
  - A **biographical sketch** may be included only if the consultant serves in a senior research capacity.

- **Research Support Staff** are individuals providing technical services in support of the research project. Include only those roles that are directly involved in the research project. Administrative, secretarial, or other general departmental or center support staff are not considered to be directly involved in the research and should **not** be listed as research support staff.
  - Do not provide biographical sketch for research support staff.

- **Administrative Support Staff** are individuals providing administrative, secretarial, or other general departmental or center support. Administrative support staff may be included in the proposed budget per OMB Circular A21 guidelines.
  - Do not provide biographical sketch for administrative support staff.

Appendix D: Cost and Expense Guidelines

The maximum duration and direct costs may not exceed the following for the RFP Pilot Studies to Examine *Hormone Concentrations of Interest for Breast Cancer Risk in California's Beef and Well Water*.

Project I:	2 years & $200,000
Project II:	2 years & $200,000

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.

1) Personnel

- The Budget Summary line item for Personnel should reflect the total cost of all individuals identified as supported by the grant and their level of effort. In the personnel section of the application, be sure to name all individuals to be supported by the grant and provide their percent effort (months devoted to the project). All paid individuals must also be listed on the budget.
- Follow the NIH Guidelines and Calculation scheme for determining Months Devoted to Project, available at the links below:
    - NIH Guidelines:
    - http://grants.nih.gov/grants/policy/person_months_faqs.htm
    - NIH Calculation Scheme: http://grants.nih.gov/grants/policy/person_months_conversion_chart.xls
- When computing salary for key personnel, use only the base salary at the applicant organization, excluding any supplementary income (e.g., clinical or consulting incomes). CBCRP does not enforce a salary cap, as long as the overall budget adheres to the costs & expenses guidelines and the amount requested stays within the allowable costs.
- The minimum "Months Devoted to Project" required for the PI is 1.2 months (= 10% FTE).

2) Student Tuition Fees, Graduate Student Stipends

- For non-fellowship awards: Graduate students may be paid as personnel and may also receive tuition remission. Tuition remission, however, will be considered compensation. The total compensation (salary plus fringe benefits plus tuition listed in this category) may not exceed $30,000 per project year (total for all students). A maximum of $10,000 per year is allowed for the combined costs of tuition/enrollment fee remission, fringe benefits, and health insurance. Stipend may be budgeted as salary (and included in the MTDC cost calculation) if the institution pays these expenses through a personnel line item.

3) Other Project Expenses

- Include expected costs for supplies and other research expenses not itemized elsewhere.
- Pooled expenses may be allowed as a direct cost at the discretion of the Program with certification of the following: 1) the project 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. Please explain any requested pooled expense requests in the budget justification.
- Advocate (s) Expenses. Include any travel, meeting, and consultation costs/fees associated with advocate engagement.

4) Equipment (Unit Cost over $5,000)

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.

5) Travel

- **Travel – RGPO Meeting:** CBCRP may organize an event requiring your travel within the funded grant period. All applicants should budget a one-time minimum expense of $400 under year 1 in the travel budget line labeled: "Travel - RGPO Meeting".
- **Travel - Project Related:** Project-related travel expenses are allowable only for travel directly related to the execution of the proposed research activities. Label such expenses as "Travel – Project Related." These expenses must be fully justified in the budget justification.
- **Travel - Scientific Meetings:** Scientific conference travel is limited to $2,000 per year (excluding a mandatory allocation of $400 in one year of the project for travel to the CBCRP Conference under Travel - RGPO Meeting). Label such expenses as "Travel-Scientific Meetings" and explain in budget justification.

6) Service Contracts and Consultants

- Both categories require additional description (Budget Justification).

7) 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. A subcontract is not allowed to have another subcontract. Requires additional description (Budget Justification).

8) INDIRECT (F&A) COSTS

- **Indirect cost policy:** Indirect costs are NOT allowed for Conference Awards. For other awards, Non-UC institutions are entitled to full F&A of the Modified Total Direct Cost base (MTDC); UC institutional F&A is capped at 30% MTDC (26% for off-campus projects).

- **Modified Total Direct Costs (MTDC)** include salaries and wages, 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) to an outside institution. MTDC does not include (indirect costs are not allowed on): capital expenditures, charges for patient care, scholarships and fellowships (including postdoctoral stipends), tuition remission and graduate student stipends, rental costs of space, equipment purchases more than $5,000 per item, the portion of each sub grant and subcontract in excess of the first $25,000, and the total cost of any subcontract from one UC to another UC campus. On a non-fellowship award, you may apply indirect costs to graduate student salary (under salary only, not as stipend) but not to tuition & fees.
- For all eligible projects that allow grantees to recover the full amount of their federally negotiated indirect cost rate agreement, grantees must also accept the full federally recognized F&A rate for all award subcontractors (except for subcontracts to another UC institution, where F&A is not allowed). If a grantee or subcontractor does not have a federally negotiated F&A rate at the time of the proposal submission, the grantee and/or subcontractor may estimate what the federally negotiated rate will be at the time of award and include this rate in the proposed budget, or may request a "De Minimis" F&A rate of 10% MTDC. A higher indirect rate that has been accepted for state or local government contract or other California grantmaker contract may be approved at the discretion of the Program Director and the Research Grants Program Office Executive Director.

- **INDIRECT COSTS ON SUBCONTRACTS**
  - The award recipient institution will pay indirect costs to the subcontractor.
  - For non-UC subcontracted partners, CBCRP will allow full F&A of the Modified Total Direct Cost (MTDC), as defined above.
  - F&A costs are not allowed for one UC institution's management of a subcontract to another UC institution.
  - The amount of the subcontracted partner's F&A costs can be added to the direct costs cap of any award type. Thus, the direct costs portion of the grant to the recipient institution may exceed the award type cap by the amount of the F&A costs to the subcontracted partner's institution.

Appendix E: Other Application-Related Policies and Pre and Post Award Requirements

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 26 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 26 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, 2020. 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) Executive Director Bart Aoki. 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.

Publications Acknowledgement and Open Access Policy

All scientific publications and other products from a RGPO-funded research project must acknowledge the funding support from UC Office of the President, with reference to CBCRP and the assigned grant ID number.

RGPO is committed to disseminating research as widely as possible to promote the public benefit. All publications based on funding received from RGPO are subject to the University's Open Access Policy. To assist the RGPO in disseminating and archiving the articles, the grantee institution and all researchers on the grant will deposit an electronic copy of all publications in eScholarship, UC's open access repository promptly after publication. Notwithstanding the above, this policy does not in any way prescribe or limit the venue of publication.

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

All CBCRP grant recipients must abide by other pre- and post-award requirements pertaining to Cost Share, Indirect Cost Rates, Monitoring & Payment of Subcontracts, Conflict of Interest, Disclosure of Violations, Return of Interest, Equipment and Residual Supplies, Records Retention, Open Access, and Reporting. 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 website: http://www.ucop.edu/research-grants-program/grant-administration/index.html.

Appendix F: Technical Tips and Contact Information

Applicants may encounter validation or submission errors due to two common issues.

1. **General Issues with Validation:**
    - Some applicants find that the system does not validate when the process is complete. Our experience is that most often this is caused by navigation away from a page before the "save" is complete. If you navigate away from a page before the "save" is complete, the information on that page will be lost. A screen refresh occurs automatically when the save is complete, and that is visible by a screen blink.

2. **Issues with Institution Profile:**
    - Some applicants have difficulty finding their institution in the database. Most California research institutions and universities are in the SmartSimple database, in addition to other organizations, particularly those that have applied to other UC programs previously.
    - Note for UC Applicants: You will need to type in "University of California" in the search box in order to see your campus listed in the dropdown list. If you have difficulty locating the database entry for your institution, please contact us using the information provided at the end of this document.
    - If your institution does not appear to be in the SmartSimple database, use the "search the IRS database" feature or contact us to have your institution added to the system.
    - Referees: If you have a referee who cannot locate their institution in the SmartSimple database or if they are from an institution outside the United States, they may select "Referee Institution" as their institution, and continue with registration and submission of their letter of reference. Contact RGPOgrants@ucop.edu to have their institution updated.

CONTACT INFORMATION

For the most up-to-date application and review cycle information refer to the following website: http://www.cbcrp.org/funding-opportunities/index.html

CBCRP and RGPO: Should you have any questions regarding your application, please contact:

- CBCRP Program Officer Nicholas Anthis at nicholas.anthis@ucop.edu or by phone 510-987-0358.

- Research Grants Program Office Contracts and Grants unit at RGPOgrants@ucop.edu or by phone at 510-987-9386 regarding SmartSimple technical assistance, application instructions and forms, and pre/post-award procedures.

The California Breast Cancer Research Program (CBCRP) is part of the Research Grants Program Office of the University of California, Office of the President.