DEPARTMENT OF DEFENSE

FISCAL YEAR 2001
BREAST CANCER RESEARCH PROGRAM
PROGRAM ANNOUNCEMENT I

February 16, 2001

Headquarters, U.S. Army Medical Research and Materiel Command
MCMR-PLF, 1077 Patchel Street
Fort Detrick, Maryland 21702-5024

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Foreword

The U.S. Army Medical Research and Materiel Command (USAMRMC) has been directed to continue the Department of Defense (DOD) Breast Cancer Research Program (BCRP). The deadline, format, and other criteria specified for proposals in this DOD fiscal year 2001 (FY01) BCRP Program Announcement are based on program objectives, public needs, and regulatory guidance.

General information on the USAMRMC can be obtained from the USAMRMC web site at http://mrmc-www.army.mil. Specific information on the DOD BCRP can be obtained from the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil. A copy of this program announcement and associated forms (except for the Proposal Cover Booklet; see Section 6 on page iii of this Foreword) also can be downloaded from the CDMRP web site at http://cdmrp.army.mil/funding/default. Information on the U.S. Army Medical Research Acquisition Activity can be obtained at http://www-usamraa.army.mil.

1. Highlights of Changes from the FY00 Program Announcement

- **Proposals for the FY01 BCRP will be requested through the publication of two separate program announcements.**
- This program announcement (Program Announcement I) is requesting proposals in the following three award mechanisms: Clinical Translational Research (CTR), Collaborative-CTR, and Breast Cancer Center of Excellence Awards. Program Announcement II is anticipated to be released in March 2001 and will request proposals in seven award mechanisms that have been requested in previous years: Idea, Clinical Bridge, Undergraduate Summer Training Program, Predoctoral Traineeships, Postdoctoral Traineeship, Career Development, and Historically Black Colleges and Universities/Minority Institutions Partnership Training Awards. There will also be a new type of award mechanism intended to attract outstanding investigators from a diversity of fields to explore new avenues in breast cancer research.
- The Breast Cancer Center of Excellence Awards replace the previous Virtual Breast Cancer Center of Excellence Awards offered in FY00. Please note the change in these awards from a focus on virtual networks for communication and information sharing to an emphasis on creating a scientific Center of Excellence in breast cancer research that utilizes these tools as needed and appropriate.
- A structured technical abstract using the headings in Appendix B, part 8, is required for all proposals.
- All foreign language transcripts must be accompanied by an English translation.
- Appendices related to Regulatory Compliance and Quality (Environmental Compliance, Research Involving Human Subjects and/or Anatomical Substances, Research Involving Animals, and Safety Program Plan) have been extensively revised.

2. Who May Apply

Individuals, regardless of ethnicity, nationality, or citizenship status, may apply through an eligible institution. Eligible institutions include for-profit, nonprofit, public, and private organizations. Examples include universities, colleges, hospitals, laboratories, companies, and agencies of local, state, and federal governments. Please refer to sections on individual mechanisms for additional eligibility criteria.

3. Receipt Deadlines

Investigators interested in applying for CTR and C-CTR Awards must submit a pre-proposal to be received no later than **March 14, 2001 at 4:00 p.m. Eastern Time**. See Sections III-E and IV-E for additional details. The receipt deadline for invited, full CTR and C-CTR Award proposals is **June 27, 2001 at 4:00 p.m. Eastern Time**. Investigators interested in applying for a Breast Cancer Center of Excellence Award must submit a Letter of Intent no later than **June 13, 2001 at 4:00 p.m. Eastern Time**. The receipt deadline for Breast Cancer Center of Excellence Award proposals is **June 27, 2001 at 4:00 p.m. Eastern Time**. See Appendix B, part 22 for additional details.

4. Timelines

The timeline for Clinical Translational Research and Collaborative-Clinical Translational Research Award proposals is:

Pre-Proposal Receipt:	**March 14, 2001 at 4:00 p.m. Eastern Time**
Pre-Proposal Screening:	April 2001
Invitation for Full Proposals:	April 2001
Full Proposal Receipt:	**June 27, 2001 at 4:00 p.m. Eastern Time**
Peer Review:	August 2001
Request for RCQ[1] Documents:	As early as 2 weeks after the completion of peer review
Programmatic Review:	November 2001
Notification:	Approximately 2 weeks after programmatic review
Award Negotiations:	Between January 2002 and September 2002

[1] Regulatory Compliance and Quality

The timeline for Breast Cancer Center of Excellence Award proposals is:

Required Letter of Intent:	**June 13, 2001 at 4:00 p.m. Eastern Time**
Proposal Receipt:	**June 27, 2001 at 4:00 p.m. Eastern Time**
Peer Review:	August 2001
Request for RCQ[1] Documents:	As early as 2 weeks after the completion of peer review
Programmatic Review:	November 2001
Notification:	Approximately 2 weeks after programmatic review
Award Negotiations:	Between January 2002 and September 2002

5. Inquiries

Questions concerning the preparation of proposals, formats, or required documentation can be addressed to the CDMRP at:

Phone: 301-619-7079
Fax: 301-619-7792
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (BCRP01)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

Applicants should submit questions regarding this program announcement via e-mail or in writing as early as possible. Every effort will be made to answer questions within 5 working days of receipt.

6. Proposal Cover Booklet (Bubble Sheet)

A Proposal Cover Booklet must be completed for each proposal according to the instructions found in Appendix C. Proposal Cover Booklets can be requested via phone, fax, e-mail, or mail at the following addresses/numbers. Please allow sufficient time for delivery by regular mail.

Phone: 301-682-5501 (8:00 a.m.-5:00 p.m. Eastern Time)
Fax: 301-682-5521
E-mail: prequest@unitedis.com
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (BCRP01)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

7. Pre-Proposal and Proposal Submission

Applicants should refer to sections on individual award mechanisms and Appendix B for appropriate submission requirements.

Send the Pre-Proposal or Proposal to:

Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (BCRP01)
1076 Patchel Street (Building 1076)
Fort Detrick, MD 21702-5024

Driving Directions to Fort Detrick

From Washington, DC

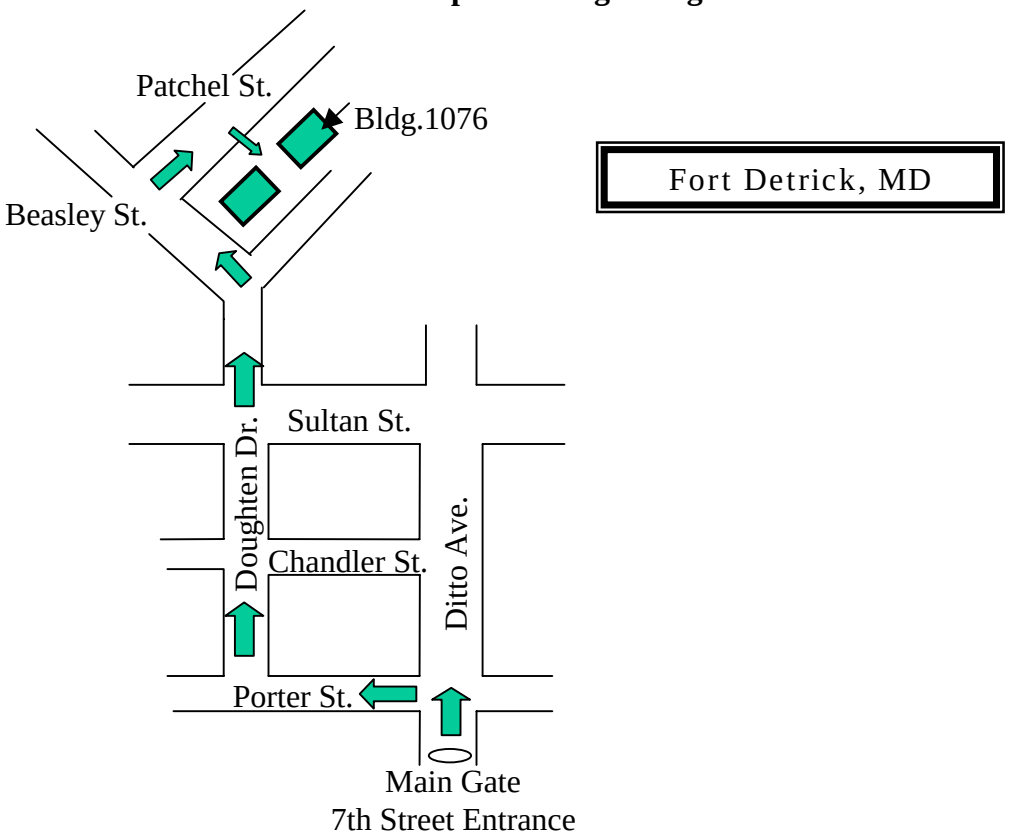
Take Interstate 495 to Interstate 270 North (exit 38) toward Rockville, Maryland. In Frederick, Interstate 270 ends and joins Route 15 North. Follow Route 15 North to the 7th Street exit. Turn right on 7th Street and proceed four blocks to Fort Detrick's Main Gate.

From Baltimore, MD

Take Interstate 695 to Interstate 70 West. In Frederick, take exit 53, Route 15 North. Follow Route 15 North to the 7th Street exit. Turn right on 7th Street and proceed four blocks to Fort Detrick's Main Gate.

Map of Fort Detrick

Packages to be delivered to the BCRP must be delivered to building 1076 as shown on the map below. To gain entry to Fort Detrick, you will be required to show your driver's license at the Main Gate. **Please allow at least 15 minutes to pass through the gate area.**



I. Overview of the Congressionally Directed Medical Research Programs

I-A. History of the Congressionally Directed Medical Research Programs

Due to increased public awareness, the success of the Department of Defense (DOD) Congressionally Directed Medical Research Programs (CDMRP), and the work of grassroots advocacy organizations, Congress has appropriated monies for peer reviewed research directed toward specific diseases. Beginning in fiscal year 1992, the U.S. Congress has directed the DOD to manage these various extra- and intramural grant programs. The U.S. Army Medical Research and Materiel Command (USAMRMC) established the CDMRP to administer these funds. To date, the USAMRMC CDMRP has received almost $2 billion targeted by Congress for peer reviewed research on breast cancer, prostate cancer, ovarian cancer, neurofibromatosis, Defense Women's Health, osteoporosis, and other specified areas.

The CDMRP exists to support research that will positively impact the health of all Americans. The CDMRP strives to identify gaps in funding and provide opportunities that will enhance program research objectives without duplicating existing funding. To meet these goals, the CDMRP has developed unique mechanisms to facilitate the funding of quality research that addresses individual program objectives.

I-B. Investment Strategy

For each program, the CDMRP has developed and refined a flexible execution and management cycle that spans the development of an investment strategy through the completion of research. A Program Staff, composed of military and civilian scientists and clinicians, manages the CDMRP. For each program, an expert Integration Panel (IP) of scientists, clinicians, and consumer advocates is convened to deliberate issues and concerns unique to the program, establish an appropriate investment strategy, and perform programmatic review as described in Section I-C.2. Based upon this investment strategy, each program then uses a variety of award mechanisms to address the most urgent needs of the research community.

I-C. Proposal Evaluation

The CDMRP uses a two-tiered review process for proposal evaluation as recommended by the National Academy of Science's Institute of Medicine. The two tiers are fundamentally different. The first tier is a scientific peer review of proposals against established criteria for determination of scientific merit. The second tier is a programmatic review of proposals that compares submissions to each other and recommends proposals for funding based on program goals.

I-C.1. Scientific Peer Review

Scientific peer review is conducted by panels organized by scientific discipline, specialty area, or award mechanism. The primary responsibility of the scientific peer review panels is to provide unbiased, expert advice on the scientific and technical merit of proposals, based upon the review criteria published for each award mechanism.

Scientific peer review panels are composed of a chair, scientific reviewers, consumer reviewers, and a nonvoting executive secretary. Selection of individuals as scientific reviewers is predicated upon their expertise as well as their varied levels of experience with scientific peer review. For the breast, prostate, and ovarian cancer research programs, consumer reviewers are cancer survivors and representatives of consumer advocacy organizations. For the neurofibromatosis research program, consumer reviewers are individuals with neurofibromatosis or their family members and representatives of consumer advocacy organizations. Consumer reviewers are nominated by an advocacy organization and are selected on the basis of their leadership skills, commitment to advocacy, and interest in science. Consumers augment the scientific peer review by bringing the patient perspective to the assessment of science and to the relevance of research.

Panel members rate each proposal based on specific evaluation criteria developed for each award mechanism (see Sections III-C, IV-C, and V-B). Two types of ratings are used. First, each of the evaluation criteria, except for the budget, is rated on a scale of 1 (lowest merit) to 10 (highest merit). This criteria scoring ensures that each component is considered in peer review. Second, the overall proposal is given a global priority score using a scale of 1 (highest merit) to 5 (lowest merit). Criteria scores are neither averaged nor mathematically manipulated to determine the global priority score. Instead, reviewers are asked to use the criteria scores as a guide in determining the global priority score. In rare instances, a proposal may be disapproved at scientific peer review if gravely hazardous or unethical procedures are involved, or if the proposal is so seriously flawed as to make its completion implausible.

The peer review summary statement is a product of scientific peer review. Each statement includes the investigator's structured technical abstract and lay (nontechnical) abstract (verbatim), the peer review scores, and an evaluation of the project as assessed by the peer reviewers according to the evaluation criteria published in this program announcement. Summary statements are forwarded to the next stage of the review process, programmatic review.

I-C.2. Programmatic Review

The second tier is programmatic review, which is accomplished by the IP. The members of the IP represent many diverse disciplines and specialty areas and are experienced with peer review procedures. Consumer advocates represent national advocacy constituencies and are full voting members of the IP. One of the functions of programmatic review is to recommend for funding a broad portfolio of proposals across all disciplines. Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool. IP

members use the peer review summary statements, which include the proposal abstracts, to review proposals. The Statement of Work may also be reviewed at this level. However, the full proposal is not forwarded to programmatic review.

The IP is committed to funding a broad-based research portfolio. The ratings and evaluations of scientific peer review panels are primary factors in programmatic review; the IP also must consider other criteria to establish this portfolio. The criteria the IP uses to make funding recommendations are:

- Ratings and evaluations of the scientific peer review panels;
- Programmatic relevance;
- Relative innovation;
- Program portfolio balance with respect to research disciplines or specialty areas; and
- Other equitable factors, e.g., adequate support for new investigators.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program are selected by the IP and recommended to the Commanding General, USAMRMC, for funding.

I-D. Notification

Following completion of the two-tiered evaluation process, every applicant will receive a letter indicating the funding status of his/her proposal, along with the peer review summary statement. Letters will be sent as official information becomes available. Thus, not all investigators will be notified at the same time.

I-E. Negotiation of the Award

Award negotiation consists of discussions, reviews, and justifications of several critical issues, including those involving Regulatory Compliance and Quality (RCQ), budget, and Statement of Work. All documents related to RCQ (environmental compliance, human subjects/anatomical substance use, animal use, and safety plan documents) will be requested in the applicant's notification letter and reviewed by RCQ staff. All proposals submitted with research involving human subjects and/or anatomical substances must be approved by the appropriate local review board. Proposals must also be approved by the U.S. Army Human Subjects Research Review Board (HSRRB). The HSRRB is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed and will require information in addition to that supplied to the local review board. Therefore, all investigators submitting such proposals must comply with the requirements detailed in the RCQ documents dealing with research

involving laboratory animals, and human subjects and/or anatomical substances **before funded research can begin.**

Concurrent with the RCQ review, a Contract Specialist from the U.S. Army Medical Research Acquisition Activity will contact the administrative representative who is authorized to negotiate contracts and grants at the applicant's institution. As part of the negotiation process, additional documentation and justifications relating to the proposed Statement of Work and associated budgets may be required.

Please note that the award start date will be determined during the negotiation process.

I-F. Annual and Final Reports

All awards will require the timely delivery of several reports during the research effort. These reports are necessary for the CDMRP to monitor progress and evaluate program outcomes. The Principal Investigator (PI) should plan on a reporting requirement consisting of:

- An **annual** report (for each year of research except the final year) that presents a detailed summary of scientific issues and accomplishments; and
- A **final** report (submitted in the last year of the award period) that details the findings and issues for the entire project.

I-G. Publications and Patents

All investigators are strongly encouraged to publish their results in the scientific literature. All publications, abstracts, and presentations must cite the DOD as the source of the research funding. For example, "This research, under Award Number DAMD…, was supported by the Department of Defense Breast Cancer Research Program, which is managed by the U.S. Army Medical Research and Materiel Command." A PI must submit to the CDMRP a copy of any manuscript or publication resulting from research funded under the award.

In accordance with the Bayh-Dole Act (35 USC[1] 200 et seq.), title to inventions and patents resulting from such federally funded research may be held by the grantee or its collaborator, but the U.S. Government shall, at a minimum, retain nonexclusive rights for the use of such inventions. An investigator must follow the instructions in the assistance agreement concerning license agreements and patents.

[1] United States Code

II. Department of Defense Breast Cancer Research Program

II-A. History of the Breast Cancer Research Program

Grass roots advocacy organizations provided the impetus that led to the fiscal year 1993 (FY93) Congressional appropriations to the Department of Defense (DOD) for $210M targeted toward breast cancer research. Since then, due to the ongoing efforts of advocacy groups and increased public awareness on health issues, Congress has continued to appropriate money for breast cancer research managed by the U.S. Army Medical Research and Materiel Command (USAMRMC) through the office of the Congressionally Directed Medical Research Programs (CDMRP). To date, Congress has appropriated more than $1.2 billion to the DOD, through the Breast Cancer Research Program (BCRP), a multidisciplinary effort aimed at the eradication of breast cancer.

A summary program history for FY92-00 appropriations of the BCRP is shown in Tables II-1 and II-2 below.

Table II-1: History of the DOD's Peer Reviewed BCRP

Program History	FY92[1]-98	FY99[2]	FY00[3]
BCRP-Managed Appropriations for Peer-Reviewed Research	$733.3M	$135M	$175M
Breast Cancer Stamp[4]	-	$1.8M	$1.3M
Number of Full Proposals Received	10,728	1,281	1,234
Number of Proposals Funded	1,806	386	~346
Percentage of Applications Recommended for Funding	17%	30%	28%
Number of Research/Infrastructure Awards[5]	1,166	221	~186
Number of Training/Recruitment Awards	640	165	~160

[1]Upon establishment of the BCRP in FY93, the CDMRP assumed responsibility for managing the $25M appropriation made in FY92 for breast cancer research that was being administered by the USAMRMC.
[2]Does not include 1,772 FY99 Concept proposals, 98 of which were awarded with FY99 funds and 206 of which are currently under negotiation with FY00 funds.
[3]Final numbers for FY00 will be available after September 30, 2001.
[4]Funds received as a result of the Stamp Out Breast Cancer Act (Public Law 105-41, H.R. 1585) are also managed under the BCRP.
[5]Includes Clinical Translational Research (CTR) and Collaborative-CTR (C-CTR) Awards.

Table II-2: Number of Proposals Received and Number of Awards Made for CTR and C-CTR Awards in FY98-00

Program History	FY97-98[1]	FY99	FY00[2]
Number of CTR and C-CTR Proposals Received			
CTR and C-CTR pre-proposals	243	87	40
CTR and C-CTR full proposals	64	22	20
Number of CTR and C-CTR Awards	10	3	~7

[1]The pre-proposal strategy was implemented in FY97.
[2]Final numbers for FY00 will be available after September 30, 2001.

II-B. Overview of the FY01 Breast Cancer Research Program: Two Program Announcements

The CDMRP is requesting proposals on breast cancer research in two separate program announcements. This program announcement (Program Announcement I) is requesting proposals in the following three award mechanisms: CTR, C-CTR, and Breast Cancer Center of Excellence Awards. Program Announcement II is anticipated to be released in March 2001 and will request proposals in seven award mechanisms that have been requested in previous years: Idea, Clinical Bridge, Undergraduate Summer Training Program, Predoctoral Traineeship, Postdoctoral Traineeship, Career Development, and Historically Black Colleges and Universities/Minority Institutions (HBCU/MI) Partnership Training Awards. There will also be a new type of award mechanism intended to attract outstanding investigators from a diversity of fields to explore new avenues in breast cancer research.

The overall goal of the FY01 BCRP is to promote research directed toward eradicating breast cancer. Within this context, the objective of the BCRP is to fund a balanced portfolio of scientifically meritorious research on all aspects of breast cancer. Proposals are sought across all areas of laboratory, clinical, behavioral, and epidemiologic research including all disciplines within the basic, clinical, psychosocial, behavioral, sociocultural, and environmental sciences; nursing; occupational health; alternative therapies; public health and policy; and economics. Additionally, proposals that address the needs of minority, low-income, rural, and other underrepresented and/or medically underserved populations are encouraged.

The USAMRMC is challenging the scientific community to design innovative research that will foster new directions for, address neglected issues in, and bring new investigators into the field of breast cancer research. As in previous years, the central theme of the BCRP is innovation. Scientific ventures that represent underinvestigated avenues of research or novel applications of existing technologies are highly sought. Although the CDMRP wishes to encourage risk-taking research, such projects must nonetheless demonstrate solid scientific judgment and rationale.

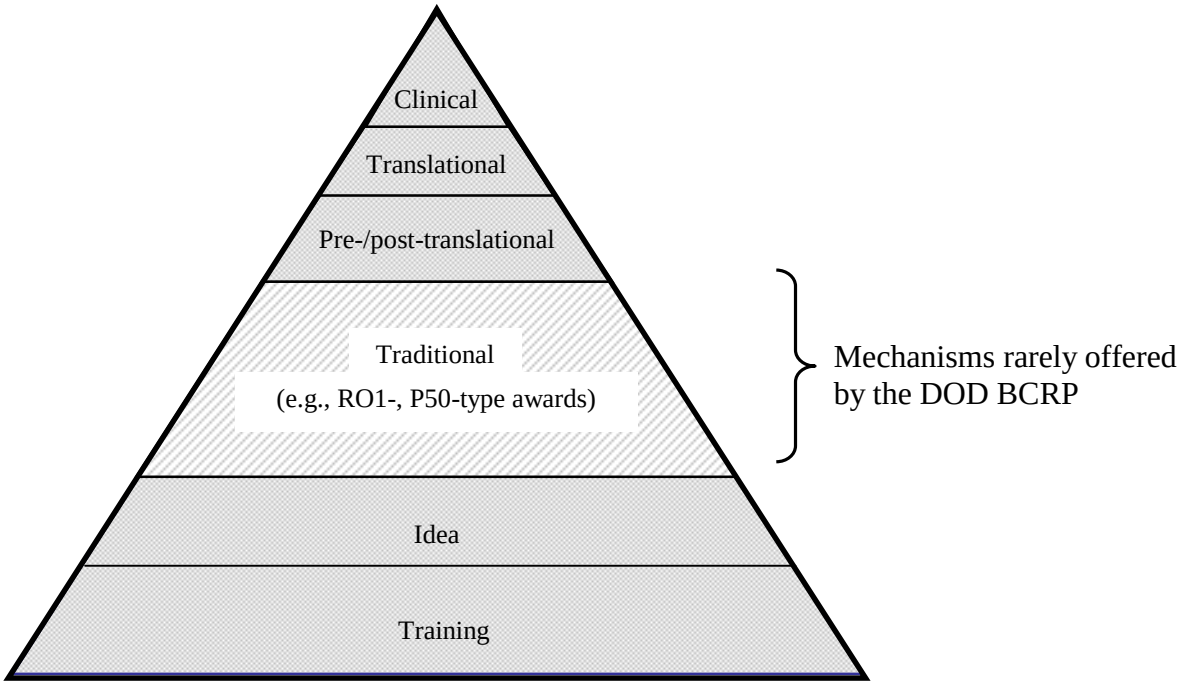
II-C. BCRP Emphasis Areas

The BCRP adapts the types of award mechanisms it offers each year to meet the current needs in breast cancer research and treatment. Mechanisms are developed based upon recommendations of the Integration Panel, an expert panel of scientists, clinicians, and consumer advocates (see Section I-B). Multiple factors are taken into consideration when designing and offering award mechanisms for each fiscal year. In particular, the BCRP factors in funding opportunities that are offered by other agencies. Award mechanisms offered each year complement and fill niches in research that are not offered/emphasized by other agencies. The BCRP funding mechanism philosophy is illustrated by the pyramid depicted in Figure II-1.

- The foundation of the pyramid is the training of investigators in breast cancer research. The FY01 BCRP will offer several training/recruitment awards (FY01 Program Announcement II, anticipated to be released in March 2001).

- The second level of the pyramid is ideas; research starts with thousands of ideas, not all of which will lead to fruitful areas of investigation. Idea Awards have been and continue to be a major emphasis of the BCRP (FY01 BCRP Program Announcement II, anticipated to be released in March 2001).

Figure II-1. BCRP Funding Philosophy



- The middle of the research pyramid is traditional research projects; these projects are often the major emphasis of a laboratory or research program. Traditional research studies are long-range and typically include studies that can be projected over several years. Traditional

research projects have not been emphasized by the DOD BCRP and are requested only in cases when there is a particular need.

- Approaching the pyramid's summit are Translational Awards. The BCRP focuses efforts at the critical juncture between bench and bedside research. Two mechanisms support these types of studies. Clinical Bridge Awards support research that is pre- or post-clinical trial (FY01 BCRP Program Announcement II, anticipated to be released in March 2001). CTR Awards support research projects that move bench research into a clinical trial during the life of the award (see Sections II-E.1 and III).

- The pinnacle of the pyramid represents the very few research studies that make it to a clinical trial. The BCRP supports the infrastructure for developing new means to perform clinical trials through C-CTR Awards (see Sections II-E.2 and IV).

Most awards offered by the BCRP fit into one level of the pyramid. However, in FY01, the BCRP is offering two new awards that may either fit a single level or span multiple levels of the pyramid.

- Breast Cancer Center of Excellence Awards may focus on an overarching problem in breast cancer research at any level of this pyramid or may traverse several levels of the pyramid from ideas to the clinic (see Section V).

- A new award mechanism will be offered that is intended to attract outstanding investigators from a diversity of fields to explore new avenues in breast cancer research (FY01 BCRP Program Announcement II, anticipated release in March 2001).

II-D. FY01 BCRP Program Announcement Award Opportunities

For the FY01 BCRP, an estimated $152M will be available to fund competitive peer reviewed breast cancer research. Approximately $50M will be used to fund proposals requested in response to BCRP Program Announcement I, while the remaining $102M will be used to fund proposals requested in response to BCRP Program Announcement II, anticipated to be released in March 2001.

The programmatic strategy for BCRP Program Announcement I is to fund proposals in two categories: (1) Research Awards and (2) Infrastructure Awards. A percentage of the available monies are allocated to fund awards at HBCU/MI. (Applicants from HBCU/MI should see Appendix B, part 1 for additional information.) In addition, as a result of the Stamp Out Breast Cancer Act (Public Law 105-41, H.R. 1585), the DOD BCRP expects to receive additional monies in 2001 for breast cancer research. The DOD plans to use all Breast Cancer Stamp monies received prior to November 2001 to fund additional scientifically meritorious proposals submitted to the FY01 BCRP.

Prospective applicants who are familiar with the CDMRP program requirements from previous years are urged to review this program announcement carefully, as revisions to award mechanism definitions and requirements have been made.

II-D.1. Research Awards

For BCRP Program Announcement I, approximately $15M will be allocated for Research Awards, which consists of CTR Awards (see Section III). CTR Awards support projects that apply promising, well-founded laboratory or other pre-clinical research to the clinical care of patients with, or populations at risk for, breast cancer.

II-D.2. Infrastructure Awards

For BCRP Program Announcement I, approximately $35M will be allocated for Infrastructure Awards, which consist of C-CTR Awards (see Section IV) and Breast Cancer Center of Excellence Awards (see Section V). The intent of C-CTR Awards is to foster the development of highly effective collaborative and consortia models to evaluate promising agents and technologies in well-designed clinical trials that utilize the combined resources of academia, the private sector, and community-based oncology clinics. The intent of Breast Cancer Center of Excellence Awards is to unite in a Center of Excellence environment the most highly qualified investigators to accelerate the solution of a major overarching problem in breast cancer research.

Reference Table of Award Mechanisms and Submission Requirements

Award Mechanism	Experience of Principal Investigator	Key Mechanism Elements	Dollars Available	Receipt Deadline	Instructions for Proposal Preparation
Clinical Translational Research Awards	All levels of experience	• Research and clinical trial components • Chemoprevention and therapeutics • Preliminary data required • Must have a clinical trial, with at least 1 year of patient accrual within the lifetime of the award	No maximum dollar limit for a period of up to 4 years	Required Pre-Proposal: March 14, 2001 4:00 p.m. ET* Full Proposal: June 27, 2001 4:00 p.m. ET	Section III
Collaborative-Clinical Translational Research Awards	All levels of experience	• To (1) develop models for performing clinical trials and (2) test new agents or technologies • Infrastructure support • To support collaborations among academia, community-based oncology clinics, and the private sector • Must contain prospective clinical trials within the lifetime of the award	A maximum award of $1.2M in direct costs for a period of up to 3 years	Required Pre-Proposal: March 14, 2001 4:00 p.m. ET Full Proposal: June 27, 2001 4:00 p.m. ET	Section IV
Breast Cancer Center of Excellence Awards	Established investigators with experience in managing large research programs	• Team of preeminent individuals from different disciplines and institutions • Unified focus on overarching breast cancer problem using a comprehensive array of personnel and resources • Accelerate research progress through communication and problem solving	A maximum award of $5M in direct costs for a period of up to 4 years	Required Letter of Intent: June 13, 2001 Full Proposal: June 27, 2001 4:00 p.m. ET	Section V

* Eastern Time

Important note regarding duplicate submissions: Submission of the same research project to the FY01 BCRP under different award mechanisms will **not** be allowed. This includes submission of the identical research project to both a Research and a Training Award mechanism. All such duplicate submissions may be administratively withdrawn. The Government reserves the right to reject any proposal.

III. Clinical Translational Research Awards

III-A. Clinical Translational Research Awards

The intent of Clinical Translational Research (CTR) Awards is to extend recent findings in breast cancer research that offer the potential to revolutionize the practice of breast cancer care. Similar to the fiscal year 2000 (FY00) solicitation for CTR proposals, **this year CTR proposals are only being sought in the areas of chemoprevention and therapeutics.** CTR Awards are for the support of projects that are likely to have a major impact on the chemoprevention and/or therapy of breast cancer by applying promising and well-founded laboratory or other pre-clinical research findings to the care of patients with, or populations at risk for, breast cancer. ***Applicants must include preliminary data to support the feasibility of their hypotheses and approaches, along with a plan to conduct a prospective clinical trial or study during the course of the award.*** The inclusion of a clear experimental and appropriately powered statistical plan to perform a prospective clinical trial or study is a requirement for consideration. Information should be provided to demonstrate that patients will be accrued for a minimum of 1 year in the proposed clinical trial during the lifetime of the award. These awards are intended to support both new and established scientists across a broad spectrum of disciplines. Ultimately, the goal of the CTR mechanism is to sponsor novel research that will result in substantial improvements over today's approach to chemoprevention and/or therapy of breast cancer.

Approximately $15M is available for CTR Awards. There are no dollar amount restrictions to these awards. Research should be completed in 4 years. As noted in Appendix F, it is the policy of the Department of Defense (DOD) that the Principal Investigator (PI) should possess the equipment needed to support the proposed research; requests for equipment in excess of 10% of the direct costs of the project will be considered only in rare cases. The focus of the CTR Award should be on the clinical trial and work leading to the clinical trial.

Investigators interested in applying for CTR Awards must submit a pre-proposal to be received **no later than March 14, 2001 at 4:00 p.m. Eastern Time** (see Section III-E for details of pre-proposal preparation). Pre-proposals will be screened according to the criteria in Section III-B to determine which projects best fulfill the intent of the award mechanism. Following completion of the pre-proposal screening process, invitations to prepare a full CTR proposal will be mailed to selected investigators no later than April 2001 (see Section III-F for details of invited, full proposal preparation). The receipt deadline for the invited, full proposal is **June 27, 2001 at 4:00 p.m. Eastern Time**. Full proposals will be evaluated in accordance with the two-tier review system and criteria described in Sections I-C, III-C, and III-D.

III-B. Screening Criteria for Clinical Translational Research Award Pre-Proposals

Pre-proposals will be screened based on the following criteria:

- The application of well-founded laboratory or other pre-clinical insights that offer the potential to revolutionize chemoprevention and/or therapy of breast cancer;
- The outline of a ***clear*** experimental plan for a prospective human clinical study or trial that will be conducted during the course of the award;
- The outline of a ***clear,*** appropriately powered statistical plan to answer the research questions posed;
- The likelihood of accruing study subjects in the proposed prospective trial for a minimum of 1 year; and
- The project's potential to extend findings in breast cancer research that offer the potential to revolutionize breast cancer chemoprevention and/or therapy.

III-C. Scientific Peer Review Evaluation Criteria for Invited, Full Clinical Translational Research Award Proposals

Invited, full CTR proposals will be evaluated in scientific peer review according to the following criteria:

- **Research Strategy:** Are the conceptual framework, hypotheses, design, methods, and analyses adequately developed and well-integrated, including laboratory and other pre-clinical evidence, to support the clinical feasibility and promise of the approach? Does the prospective clinical trial at least begin to investigate the impact on chemoprevention and/or therapy within the lifetime of the grant? Does the applicant acknowledge potential problem areas and consider alternative approaches? Does the applicant demonstrate the ability to accrue a sufficient number of subjects?
- **Translational Potential:** ***Is the project likely to result in subject accrual in the proposed prospective trial so that a minimum of 1 year of subject accrual can be achieved, presumably in the final year of the grant?*** Does the project apply promising and well-founded laboratory or other pre-clinical research findings to the care of patients with, or populations at risk for, breast cancer? Does the project form a bridge between laboratory and other pre-clinical findings and a prospective clinical trial? Does the research have the potential to result in substantial improvements over today's approach to the chemoprevention and/or therapy of breast cancer?

- **Clinical Relevance and Impact:** Is the project likely to extend recent findings in breast cancer research that offer the potential to revolutionize the practice of breast cancer care? Does the study address an important problem related to the chemoprevention and/or therapy of human breast cancer? If the aims of the application are achieved, are they likely to have a ***substantial clinical impact***?

- **Innovation:** Does the research employ ***novel*** concepts, approaches, or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new, underexplored, or unexplored areas?

- **Statistical Plan:** Is the design of the clinical trial sound and sufficiently well-developed with the ***required statistical power*** to lead to meaningful results? Is there a clear statistical plan, including power analysis, outlined in the proposal? Is the appropriate statistical expertise represented on the research team?

- **Personnel:** Is the PI appropriately trained and well-suited to carry out this work? Are the other scientific personnel well-qualified to participate in the project? Is there representation from all the areas of expertise needed to conduct the study successfully?

- **Environment:** Is the scientific environment an appropriate setting for the proposed research? Are the pre-clinical and clinical requirements adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed? Is there evidence of institutional support?

- **Budget:** Is the budget reasonable for the research proposed?

III-D. Programmatic Review Evaluation Criteria for Invited, Full Clinical Translational Research Award Proposals

Funding recommendations are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the CTR Award mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

III-E. Pre-Proposal Preparation

The following pre-proposal preparation information is specific for CTR Awards. Please note that the body of the pre-proposal is limited to **2 pages** and that the **receipt deadline is March 14, 2001 at 4:00 p.m. Eastern Time**. Following completion of the pre-proposal screening process, investigators selected to submit a full proposal will be notified no later than April 2001. The receipt deadline for the invited, full CTR proposal is **June 27, 2001 at 4:00 p.m. Eastern Time** (see Section III-F for details on invited, full CTR proposal preparation).

1. Who May Apply – See Appendix B, part 1.

2. Pre-Proposal Acceptance Criteria – See Appendix B, part 2.
   Please note that the same acceptance criteria are applied to pre-proposals as full proposals.

3. Pre-Proposal Cover Booklet – **Not required** for pre-proposals.

4. The Pre-Proposal Title Page should include the following information:

   a. Pre-Proposal title

   b. Award Category; i.e., CTR

   c. PI's full name, including middle initial

   d. PI's phone number, fax number, and e-mail address

   e. Organization name and location (including city, state, zip or postal code, and country)

   f. Three key words that describe the research (please do not use "breast cancer," "clinical trial," or "translational" as key words)

5. Pre-Proposal Translatability Statement – Limited to 1 page.
   Applicants should state explicitly how the proposed work is translatable, i.e., how it will result in a prospective clinical trial with at least 1 year of patient accrual during the course of the award. Articulate how the proposed work will further the program's goals and meet the intent of the CTR Award mechanism.

6. Pre-Proposal Body – Limited to **2 pages**.
   It is the responsibility of the investigator to ***articulate clearly how the proposed research specifically addresses the screening criteria for pre-proposals***.

7. References – Limited to 1 page.
   List all relevant references using a standard reference format that includes the full citation (i.e., authors, year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

8. Biographical Sketches – See Appendix E.
   Biographical sketches should be prepared for key personnel, including collaborating investigators. Biographical sketches may not exceed 3 pages per individual. The Biographical Sketch form can be found in Appendix E, or downloaded from the CDMRP web site at http://cdmrp.army.mil/funding/default

9. Submit the following documentation to the address listed below:

Pre-Proposal:	**ONE** clearly labeled original (binder-clipped) and **THIRTY** collated photocopies (stapled or binder-clipped) of the **entire package. Every copy must match the original.** Do not use rubber bands, or spiral or three-ring binders.
Packaging:	Package only **ONE** complete pre-proposal submission (original plus thirty copies) per box. If acknowledgment of pre-proposal receipt is desired, enclose a self-addressed, stamped postcard with each submission. This postcard should state the pre-proposal title and PI's name.
Noncompliance:	Noncompliance to established guidelines may be perceived as an attempt to gain an unfair competitive advantage and therefore may result in pre-proposal rejection. Administrative reasons for **rejection** of all or part of pre-proposals most frequently result from **failure to adhere to timelines, page limits, and font requirements.**
Send the pre-proposal to:	Commander U.S. Army Medical Research and Materiel Command ATTN: MCMR-PLF (BCRP-01) 1076 Patchel Street (Building 1076) Fort Detrick, MD 21702-5024

10. Receipt Deadline
    Please note that the **receipt deadline for CTR Award pre-proposals is March 14, 2001 at 4:00 p.m. Eastern Time.**

III-F. Invited, Full CTR Proposal Preparation

Investigators interested in applying for CTR Awards must submit a pre-proposal (see Section III-E). Pre-proposals will be screened according to the criteria in Section III-B to determine which projects best fulfill the intent of the award mechanism. Following completion of the pre-proposal screening process, invitations to prepare a full CTR proposal will be mailed to selected investigators no later than April 2001. ***Do not submit a full CTR proposal unless a letter of invitation is received following the pre-proposal screening process.*** (For the funding history of CTR proposals for fiscal years 1997-2000, please see Table II-2.)

Instructions for proposal preparation for all award mechanisms are found in Appendix B. The following supplemental information is specific for CTR Awards. Additional guidance for proposal preparation may be gained by reviewing the peer and programmatic review criteria listed in Sections III-C and III-D. Please note that the body of the proposal is limited to **15**

pages, inclusive of any figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn prior to peer review.** Ensure that the proposal is received by **June 27, 2001 at 4:00 p.m. Eastern Time.**

1. Who May Apply – See Appendix B, part 1.

2. Proposal Acceptance Criteria – See Appendix B, part 2.

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Cover Booklet – See Appendix B, part 4 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.

6. Table of Contents – See Appendix B, part 6.
   Use the table of contents at the end of this section in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.
    CTR Award applicants should state explicitly, within the 1-page limit, how the proposed work is translational, meets the intent of the CTR Award mechanism, and is relevant to breast cancer chemoprevention and/or therapeutics.

11. Proposal Body – See Appendix B, part 11.
    The body of CTR Award proposals is limited to **15 pages.**

    Describe the overall project using the *general* outline provided below.

    a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to the proposal. Cite relevant literature references.

    b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

    c. Objectives: State concisely the specific aims and research strategy of the study.

d. Preliminary Data: Provide pertinent data to support the hypothesis to be tested.

e. Proposed Research and Methods: Provide details about the experimental design and methodology, including reagents, assay validation, statistical analysis, potential pitfalls, and alternative approaches. Describe the plans for the prospective human clinical trial. If the methodology is new or unusual, describe it in sufficient detail for evaluation.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14 and Appendix E.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.

17. Administrative Documentation – See Appendix B, part 17.
In addition to the documentation described in Appendix B, include letters of support documenting availability and quality control for all critical reagents in every copy of the CTR Award proposal submission.

18. Detailed Cost Estimate – See Appendix B, part 18 and Appendix F.
Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. Please provide complete justification for expenses in all categories. There are no dollar amount restrictions for CTR Awards. Funding is to support research for up to 4 years. As noted in Appendix F, it is the policy of the DOD that the PI possess the equipment needed to support the proposed research. Requests for equipment in excess of 10% of the direct costs of the project will be considered only in rare cases. The amount allotted for travel is $1,800 per year to attend scientific/technical meetings. In addition, funding should also be requested for a one-time, 3½-day meeting to be held in the Baltimore, MD/Washington, DC area to disseminate the results of DOD-sponsored research. Applicants are asked to budget for this meeting in year 3 of the Detailed Cost Estimate form.

19. Instruments – See Appendix B, part 19.

20. Publications and Patent Abstracts – See Appendix B, part 20.

21. Proposal Submission – See Appendix B, part 21.

22. Receipt Deadline – See Appendix B, part 22.
Do not submit a full CTR proposal unless you receive a letter of invitation following the pre-proposal screening process. Please note that the **receipt deadline for invited,**

full CTR Award proposals is June 27, 2001 at 4:00 p.m. Eastern Time. Receipt of a proposal after the deadline may be grounds for proposal rejection.

23. Regulatory Compliance and Quality Requirements – See Appendix B, part 23.

Principal Investigator:_____
Last Name *First Name* *MI*

Proposal Title:_____

_____

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IV. Collaborative-Clinical Translational Research Awards

IV-A. Collaborative-Clinical Translational Research Awards

The goals of this award mechanism are (1) to support the infrastructure costs (primarily personnel) required to develop consortium models based on new or existing networks that include academic centers, community-based oncology practices, consumer/survivor groups, and the private sector for the express purpose of performing clinical trials and (2) to test new agents or technologies to accelerate the eradication of breast cancer.

Collaborative-Clinical Translational Research (C-CTR) Awards are being offered specifically to support the development of the infrastructure required to facilitate the performance of well-designed clinical trials through consortium models to evaluate promising drugs and technologies for the early detection, treatment, and prevention of breast cancer. These awards should clearly enhance patient participation in clinical trials by bringing together the resources of academia (i.e., medical centers), community-based oncology practices, and the private sector to translate promising new agents and technologies to accelerate the eradication of breast cancer. ***This award is not intended to replace, supplement, duplicate, or compete with traditional academic/community research efforts such as the National Cancer Institute-supported cooperative groups, CCOPs (Community Clinical Oncology Programs), or CGOPs (Cooperative Group Outreach Programs).*** Funds from C-CTR Awards are not intended to replace funds provided by industry to support clinical trials of new agents.

Models for performing breast cancer clinical trials through novel partnerships are the focus of C-CTR Awards. These models must specifically address the following needs: (1) decrease the time to perform a clinical trial; (2) increase the participation of patients with, and populations at risk for, breast cancer in clinical trials by making clinical trials more accessible through community oncologists and the involvement of consumer/survivor organizations; and (3) increase the number of drugs, modalities (including biological agents), or technologies tested for breast cancer. Also, applicants should form collaborations with consumer/survivor organizations in the hope that this will increase patient accrual in the planned clinical trials. Please note that breast cancer consumer/survivor groups should be active participants in these efforts. Consumers should be involved in program conception and design, recruitment of research participants, and/or in program evaluation and dissemination of information to the public. C-CTR Awards will provide funds to bring together all the necessary parties to develop and execute clinical trials that will be performed through the support of infrastructure. The proposal, in addition to providing a clear plan for the creation of the infrastructure to support the appropriate breast cancer clinical trials, must plan to test multiple novel drugs, modalities, or technologies during the award period. It is anticipated that these approaches will involve drugs, modalities, and technologies in development by the private sector (e.g., pharmaceutical, biotechnology, or other companies). Full proposals must include a letter of support that clearly demonstrates a commitment from any such partner (e.g., a pharmaceutical company providing access to new drugs/modalities/treatments/diagnostics).

The following items are essential for a C-CTR Award:

1. Drugs, modalities, or technologies ready for clinical trials (Phase I or II) with appropriate scientific hypothesis and plan;

2. A central institution coordinating a program that will include community-based oncology practices, the private sector, academic center(s), and consumer/survivor organizations;

3. Community-based oncology practices with sufficient patient populations willing to participate; and

4. A clear plan to provide the required personnel, financial resources, and coordination at the level necessary to conduct the proposed trials.

At the completion of the funding period, the project must be able to demonstrate the following:

1. The testing of novel drugs, modalities, or technologies in well-designed prospective ***clinical trials*** with appropriate hypotheses, the outcomes of which clearly demonstrate increased efficiency, patient enrollment, and participation of community-based oncologists and patients over existing models for performing clinical trials;

2. The successful development of a novel collaboration or consortium that includes academic center(s), community-based oncology practices, consumer/survivor organizations, and the private sector to execute clinical trials that can efficiently accrue patients; and

3. Significant patient accrual and demonstrable results from clinical trials of multiple drugs, modalities, or technologies.

The following issues also should be considered when applying for C-CTR Awards:

1. The C-CTR is not an appropriate funding mechanism for pre-clinical drug, modality, or technology development.

2. Proposals should include data on pre-clinical results that clearly demonstrate that the drugs, modalities, or technologies are ready to be tested in clinical trials.

3. A requirement for consideration will be the inclusion of a clear experimental and statistical plan to perform ***prospective*** clinical trials.

Approximately $5M is available to support C-CTR awards. Support can be requested for a maximum of $1.2M in direct costs for a period of up to 3 years, plus indirect costs as appropriate. Direct costs can support clinical research nurses and/or data management personnel for clinical data management and clinical outreach. Funds are not intended to support direct patient costs. Applicants are encouraged to increase the effective resource base for these studies by developing partnerships with private industry for additional funding support. As noted in

Appendix F, it is the policy of the Department of Defense (DOD) that the Principal Investigator (PI) should possess the equipment needed to support the proposed research; requests for equipment in excess of 5% of the direct costs of the project will be considered only in rare cases.

Investigators interested in applying for a C-CTR Award must submit a pre-proposal to be received **no later than March 14, 2001 at 4:00 p.m. Eastern Time** (see Section IV-E for details of pre-proposal preparation). Pre-proposals will be screened according to the criteria in Section IV-B to determine which projects best fulfill the intent of the award mechanism. Following completion of the pre-proposal screening process, invitations to prepare a full C-CTR proposal will be mailed to selected investigators no later than April 2001 (see Section IV-F for details of invited, full proposal preparation). The receipt deadline for the invited, full proposal is **June 27, 2001 at 4:00 p.m. Eastern Time**. Full proposals will be evaluated in accordance with the two-tier review system and criteria described in Sections I-C, IV-C, and IV-D.

IV-B. Screening Criteria for Collaborative-Clinical Translational Research Award Pre-Proposals

Pre-proposals will be screened based on the following criteria:

- The development of a clear collaboration among academic medical center(s), community-based oncology practices, the private sector, and consumer/survivor organizations with one organization acting as the coordinating institution;

- Evidence to clearly show that the drugs, modalities, or technologies are ready for clinical trials;

- The application of well-founded laboratory or other pre-clinical findings to the prevention, detection, diagnosis, or treatment of patients with, or populations at risk for, breast cancer;

- The outline of a ***clear*** experimental plan to perform peer-reviewed prospective human clinical trials;

- Documentation of sufficient patient populations willing to participate in prospective clinical trials and potential for significant patient accrual;

- The identification of appropriate statistical support;

- The likelihood of obtaining initial clinical results within the lifetime of the award;

- An explanation of why the proposed model is expected to accelerate the translation of new agents or technologies into clinical practice to support the eradication of breast cancer, and the project's potential to have a ***major impact*** on breast cancer prevention, detection, diagnosis, and/or treatment.

IV-C. Scientific Peer Review Evaluation Criteria for Invited, Full Collaborative-Clinical Translational Research Award Proposals

Invited, full C-CTR proposals will be evaluated in scientific peer review according to the criteria listed below.

- **Consortium Model:** Are the partners capable and committed? Are the collaborations likely to lead to increased patient accrual? Does the proposed network of collaborations represent an innovative model for early clinical trials? Are the private sector, community-based oncology practices, and consumer/survivor organizations active participants in this effort as demonstrated by letters of commitment? Is there evidence of institutional support for the establishment of the consortium?

- **Available Agents or Technology:** Does the applicant ***clearly*** demonstrate sufficient evidence that multiple drugs, modalities, or technologies are available for testing in clinical trials? Are the agents to be tested ones that would provide new insights into the prevention, detection, diagnosis, and/or treatment of breast cancer?

- **Research Strategy:** ***Has a well-designed plan been developed to test multiple agents in prospective clinical trials within the lifetime of the award***? Are the plans for patient accrual realistic, including demonstration of the availability of sufficient patient populations? Has the ethnic diversity of the patient population been considered appropriately in developing community collaborations?

- **Translational Potential:** ***Is the project likely to produce meaningful clinical results within the course of the award***? Does the project apply promising and well-founded laboratory or other pre-clinical research findings to the care of patients with, or populations at risk for, breast cancer? Does the collaborative model have the potential to result in substantial improvements over today's approaches to translating new agents and technologies into new strategies for the prevention, detection, diagnosis, and/or treatment of breast cancer?

- **Clinical Relevance and Impact:** Does this study address an important problem related to the prevention, detection, diagnosis, and/or treatment of human breast cancer? If the aims of the application are achieved, are they likely to have ***a significant impact on the prevention, early detection, and/or treatment of breast cancer***?

- **Innovation:** Does the consortium employ ***novel*** concepts, approaches, or methods? Are the aims original and innovative? Are the proposed collaborations a novel way to perform clinical trials? Does the project challenge existing paradigms or develop new, underexplored, or unexplored areas?

- **Statistical Plan:** Is the design of the clinical trials sound and sufficiently well-developed with the ***required statistical power*** to lead to meaningful results? Is there a clear statistical plan including power analysis outlined in the proposals? Is the appropriate statistical expertise represented in the research team?

- **Personnel:** Is the PI appropriately trained and well-suited to carry out and coordinate this work? Are the other personnel well-qualified to participate in the project? Is there representation from all the areas of expertise needed to conduct the study successfully? Does the supporting documentation demonstrate the ability of all participants to execute the project goals successfully? Has a plan been presented for how this project will be managed and coordinated?

- **Budget:** Is the budget reasonable for the research proposed?

IV-D. Programmatic Review Evaluation Criteria for Invited, Full Collaborative-Clinical Translational Research Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the C-CTR mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

IV-E. Pre-Proposal Preparation

The following pre-proposal preparation information is specific for the C-CTR Award mechanism. Please note that the body of the pre-proposal is limited to **3 pages** and that the **receipt deadline is March 14, 2001 at 4:00 p.m. Eastern Time**. Following completion of the pre-proposal screening process, investigators selected to submit a full proposal will be notified no later than April 2001. The receipt deadline for the invited, full C-CTR proposal is **June 27, 2001 at 4:00 p.m. Eastern Time** (see Section IV-F for details on invited, full C-CTR proposal preparation).

1. Who May Apply – See Appendix B, part 1.

2. Pre-Proposal Acceptance Criteria – See Appendix B, part 2.
   Please note that the same acceptance criteria are applied to pre-proposals as full proposals.

3. Pre-Proposal Cover Booklet – **Not required** for pre-proposals.

4. The Pre-Proposal Title Page should include the following information:

   a. Pre-Proposal title

   b. Award Category; i.e., C-CTR

   c. PI's full name, including middle initial

d. PI's phone number, fax number, and e-mail address

e. Organization name and location (including city, state, zip or postal code, and country)

f. Three key words that describe the research (please do not use "breast cancer," "clinical trial," or "translational" as key words)

5. Pre-Proposal Body – Limited to **3 pages**.
   It is the responsibility of the investigator to clearly articulate how the proposed research meets the pre-screening criteria. At least 1 page should be dedicated to outlining the community clinic participation.

6. References – Limited to 1 page.
   List all relevant references using a standard reference format that includes the full citation (i.e., authors, year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

7. Biographical Sketches – See Appendix E.
   Biographical sketches should be prepared for key personnel, including a collaborating investigator at each community clinic. Biographical sketches may not exceed 3 pages per investigator. The Biographical Sketch form can be found in Appendix E, or it can be downloaded from the CDMRP web site at http://cdmrp.army.mil/funding/default

8. Submit the following documentation to the address listed below:

Pre-Proposal:	**ONE** clearly labeled original (binder-clipped) and **THIRTY** collated photocopies (stapled or binder-clipped) of the **entire package. Every copy must match the original.** Do not use rubber bands, or spiral or three-ring binders.
Packaging:	Package only **ONE** complete pre-proposal submission (original plus thirty copies) per box. If acknowledgment of pre-proposal receipt is desired, enclose a self-addressed, stamped postcard with each submission. This postcard should state the pre-proposal title and PI's name.
Noncompliance:	Noncompliance to established guidelines may be perceived as an attempt to gain an unfair competitive advantage and therefore may result in pre-proposal rejection. Administrative reasons for **rejection** of all or part of pre-proposals most frequently result from **failure to adhere to timelines, page limits, and font requirements.**

Send the pre-proposal to: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (BCRP-01)
1076 Patchel Street (Building 1076)
Fort Detrick, MD 21702-5024

9. Receipt Deadline
   Please note that the **receipt deadline for C-CTR Award pre-proposals is March 14, 2001 at 4:00 p.m. Eastern Time.**

IV-F. Invited, Full C-CTR Proposal Preparation

Investigators interested in applying for C-CTR Awards must submit a pre-proposal (see Section IV-E). Pre-proposals will be screened according to the criteria in Section IV-B to determine which projects best fulfill the intent of the award mechanism. Following completion of the pre-proposal screening process, invitations to prepare a full C-CTR proposal will be mailed to selected investigators no later than April 2001. ***Do not submit a full CTR proposal unless a letter of invitation is received following the pre-proposal screening process.*** (For the funding history of C-CTR proposals for fiscal years 1997-2000, please see Table II-2.)

Instructions for proposal preparation for all award mechanisms are found in Appendix B. The following supplemental information is specific for C-CTR Awards. Additional guidance for proposal preparation may be gained by reviewing the peer and programmatic review criteria listed in Sections IV-C and IV-D. Please note that the body of the proposal is limited to **15 pages**, inclusive of any figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn prior to peer review.** Ensure that the proposal is received by **June 27, 2001 at 4:00 p.m. Eastern Time.**

1. Who May Apply – See Appendix B, part 1.

2. Proposal Acceptance Criteria – See Appendix B, part 2.

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Cover Booklet – See Appendix B, part 4 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.

6. Table of Contents – See Appendix B, part 6.
   Use the table of contents at the end of this section in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.
    C-CTR Award applicants should state explicitly, within the 1-page limit, how the model specifically addresses the following needs: (1) decrease the time to perform a clinical trial; (2) increase the participation of patients with, and populations at risk for, breast cancer in clinical trials by making clinical trials more accessible through community oncologists and the involvement of consumer/survivor organizations; and (3) increase the number of drugs, modalities (including biological agents), or technologies tested for breast cancer.

11. Proposal Body – See Appendix B, part 11.
    The body of C-CTR Award proposals is limited to **15 pages.**

    Describe the overall project using the *general* outline provided below.

    a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to the proposal. Cite relevant literature references.

    b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

    c. Objectives: State concisely the specific aims and research strategy of the study.

    d. Preliminary Data: Proposals should include data on pre-clinical results that clearly demonstrate that the drugs, modalities, or technologies are ready to be tested in clinical trials (Phase I or II).

    e. Proposed Research and Methods: This section should include, but is not limited to,

        i. A description of collaboration among community-based oncology practices, the private sector, academic center(s), and consumer survivor group(s);

        ii. A description of how the central institution will coordinate the program;

        iii. Information on patient populations;

        iv. A clear plan to provide the required personnel, financial resources, and coordination at the level necessary to conduct the proposed trials; and

v. A plan to test multiple agents in *prospective* clinical trials within the lifetime of the award. Provide details about the statistical plan, experimental design and methodology, including reagents, assay validation, statistical analysis, potential pitfalls, and alternative approaches. If the methodology is new or unusual, describe it in sufficient detail for evaluation.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14 and Appendix E.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.

17. Administrative Documentation – See Appendix B, part 17.
    On the list of all items included in the Administrative Documentation section, (see Appendix B), include the names, position, and grant function (e.g., private sector collaborator, breast cancer consumer/survivor organizations) of the authors of all letters of support.

    The following documentation must also be included in every copy of the C-CTR Award proposal submission:

    - Letters from private sector collaborators documenting a willingness to participate and the availability of the necessary drugs, modalities, or technologies.

    - Letters from academic center collaborators, if any, documenting a willingness to participate and, if appropriate, access to patient populations and the availability of the necessary drugs, modalities, or technologies.

    - Letters from community-based oncology practices documenting a willingness to participate and access to patient populations.

    - Letters from breast cancer consumer/survivor organizations documenting a willingness to participate and how they will contribute to the projects, e.g., through increasing patient accrual, program conception and design, recruitment of research participants, and/or in program evaluation and dissemination of information to the public.

18. Detailed Cost Estimate – See Appendix B, part 18 and Appendix F.
    Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. Please provide complete justification for expenses in all categories. The cost of preparing proposals in response to these instructions is not considered an allowable direct charge to any resultant award. Support

can be requested for a maximum of $1,200,000 in direct costs for a period of up to 3 years, plus indirect costs as appropriate. Direct costs can support infrastructure costs (primarily personnel), including clinical research nurses and/or data management personnel for clinical data management and clinical outreach. Funds are not intended to replace funds provided by industry to support clinical trials of new patients or to support direct patient costs. Applicants are encouraged to increase the effective resource base for these studies by developing partnerships with private industry for additional funding support. As noted in Appendix F, it is the policy of the DOD that the PI should possess the equipment needed to support the proposed research; requests for equipment in excess of 5% of the direct costs of the project will be considered only in rare cases. The amount allotted for travel is $1,800 per year per collaborator to attend scientific/technical meetings. In addition, funding should also be requested for the PI for a one-time, 3½-day meeting to be held in the Baltimore, MD/Washington, DC area to disseminate the results of DOD-sponsored research. Applicants are asked to budget for this meeting in year 3 of the Detailed Cost Estimate form.

19. Instruments – See Appendix B, part 19.

20. Publications and Patent Abstracts – See Appendix B, part 20.

21. Proposal Submission – See Appendix B, part 21.

22. Receipt Deadline – See Appendix B, part 22.
Do not submit a full C-CTR proposal unless you receive a letter of invitation following the pre-proposal screening process. Please note that the **receipt deadline for invited, full C-CTR Award proposals is June 27, 2001 at 4:00 p.m. Eastern Time. Receipt of a proposal after the deadline may be grounds for proposal rejection.**

23. Regulatory Compliance and Quality Requirements – See Appendix B, part 23.

Principal Investigator:_____
Last Name *First Name* *MI*

Proposal Title:_____

_____

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V. Breast Cancer Center of Excellence Awards

V-A. Breast Cancer Center of Excellence Awards

Note: The Breast Cancer Center of Excellence Award replaces the previous Virtual Breast Cancer Center of Excellence Award offered in 2000. Please note the change in these awards from a focus on virtual networks for communication and information sharing to an emphasis on creating a scientific Center of Excellence in breast cancer research that utilizes these tools as needed and appropriate.

The intent of the Breast Cancer Center of Excellence Awards (BCCOE or Center) is to unite in a Center of Excellence environment the most highly qualified investigators to accelerate the solution of a major overarching problem in breast cancer research. A BCCOE must have a ***unified focus*** on an important question relevant to breast cancer. The BCCOE Awards are intended to support the establishment of a directed multi-institutional collaboration among highly accomplished scientists from diverse backgrounds and areas of expertise to create a critical mass of talent focused on a well-defined scientific problem. Breast cancer consumer/survivor groups should be active participants in these multidisciplinary efforts. The results generated from these awards should have a major impact on the prevention, detection, diagnosis, and/or treatment of breast cancer. ***This award is not intended to replace, supplement, duplicate, or compete with other collaborative research efforts such as the National Cancer Institute-supported Specialized Programs of Research Excellence (SPORE) or Program Project grants,*** which may be more narrow in focus as in the case of the Program Project grants, or broader as in the case of the SPORE grants.

Proposals for the BCCOE Award should (1) assemble and integrate a team of accomplished investigators from different disciplines and institutions; (2) focus on the solution of an important problem in breast cancer research using research strategies that employ the Center's comprehensive array of personnel and resources; and (3) generally facilitate and accelerate research progress through real-time communication and team problem solving. In setting up a BCCOE, emphasis should be placed on attracting preeminent scientists in the targeted areas of research, promising young investigators, and individuals from complementary fields who ultimately represent the right team to solve the problem(s) identified. Communication between BCCOE team members should be addressed, including sharing data in real time and use of information technologies to facilitate timely and effective communication and cooperation. It is anticipated that in order to meet the requirement to bring together the most qualified team of investigators to address a specific problem, the BCCOEs will be multi-institutional, unless a justification is provided that a single institution can best address the Center's focus. Consumers should be members of the collaborative team and should be involved in program conception and design, discussions, recruitment of research participants, and/or program evaluation and dissemination of information to the public. Collaborations established through the Center should result in a synergistic research program with a central, unified theme to address a specific research question rather than an additive set of subprojects. Collaborators may plan to meet in person two to four times per year to assess research progress, address problems, and define future directions.

BCCOE Award proposals should address an overarching problem that is relevant to the prevention, detection, diagnosis, and/or cure of breast cancer. The central problem addressed by the Center should (1) solve a major problem(s) in breast cancer research; (2) develop critically needed resources (e.g., databases to address specific problems); and/or (3) create a unique, new approach or infrastructure to focus on a critical research problem. BCCOE Award proposals are sought across all areas of laboratory, clinical, behavioral, and epidemiological research, including basic, clinical, psychosocial, behavioral, sociocultural, and environmental sciences; nursing; occupational health; alternative therapies; public health and policy; and economics. **The BCRP is especially interested in funding proposals in the areas of (1) prevention, (2) development of markers for early detection, (3) development of novel chemopreventive and therapeutic agents and/or strategies, (4) improving clinical practice, and (5) alternative medicine**. The following list illustrates topics that the BCRP believes may be appropriate for the focus of these awards. This list is meant only to provide examples and should not be considered either comprehensive or as examples of preferred or more desirable research questions. Pertinent topics might include:

- Accelerating the development of specific breast cancer chemopreventives or prevention strategies (e.g., new chemopreventive agents, natural products, or behavior modification strategies). Problems that such a Center might address include the development of acceptable array(s) of breast cancer markers for use as surrogate endpoints in clinical trials of new preventive agents or the development of new, innovative pre-clinical and/or clinical models.

- Determining the potential role of specific environmental factors in breast cancer etiology (e.g., studying and categorizing interactions of environmental factors with specific breast cancer genes and/or molecular pathways).

- Pursuing a common basic or translational research problem that has reached a stage where linking the participants from several laboratories through a BCCOE would avoid unnecessary duplication, resolve discrepancies, and accelerate and facilitate progress in areas relevant to breast cancer (e.g., erbB/erbB receptor family signaling, BRCA I/II action, steroid hormone co-stimulators).

- Generating large or diverse databases through epidemiological studies that link population data in order to determine risk factors or evaluate outcomes in breast cancer (e.g., dietary contributions, interactions of genes with known risk factors, quality of life assessment of therapies).

- Creating a direct digital breast imaging database that would be readily available on-line as a centralized national resource, which would facilitate rapid technological advances that could revolutionize the diagnosis of breast cancer.

- Undertaking breast cancer detection studies that extend across scientific disciplines, such as breast cancer detection aids (computer or human), development of detection performance metrics, lesion characterization, individualized risk assessment, and development of management strategies for patients in different risk categories.

Communication and the overall organization and management of the Centers are important aspects of the BCCOE Award proposals. The management and communication components should provide the basis for organizing and managing the Center, establish the processes and tools for regular and systematic communication, data management, project meetings and other issues of common concern. It is anticipated that the BCCOE could take advantage of powerful Internet and current electronic communication tools, as well as formal and informal meetings.

The topic chosen should be one that is best addressed by a multidisciplinary team of experts. The Center should maximize the utilization of resources and minimize unnecessary duplication; e.g., experimental techniques, databases, models (including animal models), antibodies, etc. should be shared resources in the Center. These awards should lead to publications with multidisciplinary authorship. The Center Director, i.e., the Principal Investigator (PI) on the proposal, should have a proven record of leadership and scientific ability to direct and oversee large research programs, including the effective use of communication tools and the management of multifaceted and multidisciplinary projects.

Projects should be based on well-founded research findings. Applicants ***must*** include published or preliminary data to support the feasibility of their hypotheses and/or approaches, along with a plan to develop the proposed center and conduct the anticipated research.

Approximately $30M is available to support BCCOE Awards. Funding for BCCOE Awards can be requested for a maximum of $5M in direct costs for a period of up to 4 years, plus indirect costs as appropriate.

For complete proposal requirements, please refer to Section V-E. Additional guidance for proposal preparation may be gained by reviewing the peer and programmatic review criteria listed in Sections V-B and V-C.

V-B. Scientific Peer Review Evaluation Criteria for Breast Cancer Center of Excellence Award Proposals

Breast Cancer Center of Excellence proposals will be evaluated in scientific peer review according to the criteria listed below:

- **Center Structure:** Does the Center offer the potential to significantly advance progress toward addressing a key question in breast cancer research? Does the team assembled in the Center represent a "critical mass" of talent and is there a unifying focus that will facilitate and accelerate progress? Does the Center unite and integrate the ***most highly qualified individuals*** to contribute to the project?

- **Scientific Relevance and Impact:** Will the Center make an original and important contribution to (1) significantly advancing research to address the key breast cancer research problem/area identified and (2) the goal of eradicating breast cancer?

- **Innovation:** Does this BCCOE represent potentially more effective and innovative approaches to better address the unifying research question(s) posed? For example, does the Center draw on expertise from other fields, employ ***novel*** approaches or methods, and/or challenge existing assumptions and paradigms?

- **Personnel:** Does the Center Director (i.e., the PI) have the appropriate qualifications and experience to oversee the research that addresses the overarching breast cancer problem proposed and to coordinate and manage the proposed Center? Is there representation from all the areas of expertise needed to conduct the study successfully? Does the team also include members who will provide new perspectives and fresh insights? Are consumer advocates active participants in the project and are their roles clearly defined? Is the contribution of each investigator clear?

- **Research Strategy:** Is the unifying research problem(s) one that would be best solved through this multidisciplinary (generally multi-institutional) approach? Does the research question provide a real basis for a unified focus? Are the conceptual framework, hypothesis, design, methods, and analyses adequately developed and well-integrated to support the feasibility and promise of the approach? Do the preliminary data cited support the rationale for the Center? Does the applicant acknowledge potential problem areas and consider alternative approaches? If needed, are statistical support services included in the Center's design?

- **Management and Communications Plan:** Is a management plan proposed to integrate and optimize the research and collaborations proposed? Does the PI have a clear strategy and plan that will ensure cross-Center participation and real-time communication of results, issues, problems, and progress? If appropriate, does the proposal utilize state-of-the-art communication tools and is a plan for data management and statistical support presented?

- **Environment:** Do the different institutions/organizations involved in this project strengthen the Center? Is the appropriate support staff available for administering all of the Center's functions (e.g., Communications infrastructure, informatics, access to required databases)? Have the institutions demonstrated their clear commitment to the Center?

- **Budget:** Is the budget reasonable for the Center and research proposed?

V-C. Programmatic Review Evaluation Criteria for Breast Cancer Center of Excellence Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the BCCOE Award mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

V-D. Letter of Intent

The BCRP would like to provide BCCOE Award applicants as much time as possible to prepare these proposals. However, because of the need to plan in advance for peer review, all applicants considering submission of a BCCOE Award proposal in response to this Program Announcement are **required to submit a Letter of Intent to be received by June 13, 2001 at 4:00 p.m. Eastern Time**, 2 weeks prior to the proposal receipt deadline. This form can be found in Appendix A and submitted as directed, or completed and submitted via the CDMRP web site at http://cdmrp.army.mil/funding/default. Please note that proposals submitted without prior submission of the required Letter of Intent may be considered noncompliant.

V-E. Proposal Preparation

Instructions for proposal preparation are found in Appendix B. The following supplemental information is specific for BCCOE Awards. Please note that the body of the proposal is limited to **25 pages**, inclusive of any figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn prior to peer review.** Ensure that the proposal is received by **June 27, 2001 at 4:00 p.m. Eastern Time.**

1. Who May Apply – See Appendix B, part 1.

2. Proposal Acceptance Criteria – See Appendix B, part 2.

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Cover Booklet – See Appendix B, part 4 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.

6. Table of Contents – See Appendix B, part 6.
   Use the table of contents at the end of this section in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.
    BCCOE Award applicants should state explicitly, within the 1-page limit, how the proposed work (1) meets the intent of the BCCOE Award mechanism; (2) will accelerate the solution of an overarching and/or multidisciplinary problem in breast cancer research; and (3) will have a major impact on the prevention, detection, diagnosis, and/or treatment of breast cancer.

11. Proposal Body – See Appendix B, part 11.
    The body of BCCOE Award proposals is limited to **25 pages.**

    Describe the overall project using the outline provided below.

    a. Background: Provide a brief statement of the ideas and reasoning behind the proposed Center. Describe the major question(s) in breast cancer research that is the focus of this proposal. Include information on previous experience most pertinent to the proposal. Cite relevant literature references.

    b. Purpose: State the purpose of the Center and the expected results and outcomes. Indicate how the Center is synergistic.

    c. Objectives: State concisely the specific aims and research strategy of the study. Describe the expected measurable outcomes of the proposed Center. Provide information as to how the Center will address these objectives and why the approaches are better than traditional collaborations.

    d. Collaborators: Provide information on the team of multidisciplinary, multi-institutional researchers and consumer advocates participating in the project and how they will contribute to the project. Describe how the team of multi-institutional, multidisciplinary researchers and consumer advocates will be organized, administrated, and managed. If the proposed Center does not involve a multi-institutional effort, provide justification that the Center's focus can best be addressed within the single institution.

    e. Data: Provide information on well-founded research that supports this project. Include data to support the feasibility of the hypotheses and/or approaches.

    f. Proposed Research and Methods: Describe the experimental plan and methodology that will address the specific research question. Provide information on how the Center will maximize the utilization of resources and minimize unnecessary duplication; e.g., experimental techniques, databases, models (including animal models), antibodies.

g. Communications: Describe the key features of the communications plan that will help expedite the proposed research. Provide information on the availability of communication network resources and support for this research. State the specific features of this plan that facilitate and encourage the real-time exchange of research findings.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14 and Appendix E.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.

17. Administrative Documentation – See Appendix B, part 17.
In addition to the documentation described in Appendix B, the following documentation must be included in every copy of the BCCOE proposal submission:

- Letters from private sector and academic center collaborators, as appropriate, documenting a willingness to participate and demonstrating that a multi-institutional, multidisciplinary team of investigators is participating in the project, that the necessary drugs, modalities, or technologies are available, and that there is no unnecessary duplication of resources.

- Letters from breast cancer consumer/survivor organizations documenting a willingness to participate and how they will contribute to the projects, e.g., through increasing patient accrual, program conception and design, recruitment of research participants, and/or in program evaluation and dissemination of information to the public.

18. Detailed Cost Estimate – See Appendix B, part 18 and Appendix F.
Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. Please provide complete justification for expenses in all categories. The cost of preparing proposals in response to these instructions is not considered an allowable direct charge to any resultant award. Funding for BCC0E Awards can be requested for a maximum of $5M in direct costs for a period of up to 4 years, plus indirect costs as appropriate. As noted in Appendix F, it is the policy of the Department of Defense (DOD) that the PI possess the equipment needed to support the proposed research. However, because the intent of this award mechanism is to establish Centers that expedite research in a critical area of breast cancer research through real-time exchange of results and information sharing, reasonable requests for

funds to purchase necessary informatics equipment will be considered. In addition to the funds for internal center meetings, the amount allotted for travel is $1,800 per year per collaborator to attend scientific/technical meetings. Funding should also be requested for the PI for a one-time, 3½-day meeting to be held in the Baltimore, MD/Washington, DC area to disseminate the results of DOD-sponsored research. Applicants are asked to budget for this meeting in year 3 of the Detailed Cost Estimate form.

19. Instruments – See Appendix B, part 19.

20. Publications and Patent Abstracts – See Appendix B, part 20.

21. Proposal Submission – See Appendix B, part 21.

22. Receipt Deadline – See Appendix B, part 22.
    Please note that the **receipt deadline for Breast Cancer Center of Excellence Award proposals is June 27, 2001 at 4:00 p.m. Eastern Time. Receipt of a proposal after the deadline may be grounds for proposal rejection.**

23. Regulatory Compliance and Quality Requirements – See Appendix B, part 23.

Principal Investigator:_____
Last Name *First Name* *MI*

Proposal Title:_____

_____

Breast Cancer Center of Excellence Award Proposal
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