

Appendix A

Letter of Intent

to Submit Proposals in Response to the
FY99 Department of Defense Ovarian Cancer Research Program Announcement

Please fill out one of these forms for each proposal you intend to submit.
Fax this form to (301) 682-5521.

Principal Investigator's Name: _____

Principal Investigator's Address: _____

Phone Number: _____

Fax Number: _____

Intended award category to which the proposal will be submitted (please check **ONLY** one):

- Idea Award
- New Investigator Award

Content area that will be addressed in the proposal. (Check no more than 5)

- | | | |
|---|--|--|
| <input type="checkbox"/> Alternative Medicine | <input type="checkbox"/> Gene Expression | <input type="checkbox"/> Prevention |
| <input type="checkbox"/> Behavioral/Social Sciences | <input type="checkbox"/> Gene Sequencing/Mapping | <input type="checkbox"/> Protein-nucleic Acid Interactions |
| <input type="checkbox"/> Biological Response Modifiers | <input type="checkbox"/> Health Care Delivery | <input type="checkbox"/> Radiologic Sciences |
| <input type="checkbox"/> Cell Biology | <input type="checkbox"/> Immunologic Sciences | <input type="checkbox"/> Surgery |
| <input type="checkbox"/> Clinical/Experimental Therapeutics | <input type="checkbox"/> Medical Genetics | <input type="checkbox"/> Technology Development |
| <input type="checkbox"/> Endocrinology | <input type="checkbox"/> Molecular Genetics | <input type="checkbox"/> Tumor Biology/Progression |
| <input type="checkbox"/> Epidemiology/Biostatistics | <input type="checkbox"/> Pathobiology | <input type="checkbox"/> Virology |
| | <input type="checkbox"/> Pharmacology/Toxicology | |

Other, please specify _____

Proposal title and brief description: _____

Use an additional page if needed. Please include the name of PI and applicant institution for tracking purposes.

Please send me the following:

- Copies of the Proposal Cover Booklet - How many? _____
- Copies of the Program Announcement - How many? _____

Appendix B

Proposal Cover Booklet Instructions

You should submit an original Proposal Cover Booklet and three photocopies. Additional Cover Booklets and instructions can be requested via fax, phone, e-mail, or mail at the addresses listed below. Please allow sufficient time for delivery by regular mail.

Fax: (301) 682-5521
Phone: (301) 682-5501
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (OCR99-Announcement)
524 Palacky Street
Fort Detrick, MD 21702-5024

ATTENTION: In order to facilitate the processing of the proposal, it is extremely important that you read and follow the instructions completely as you are filling out the Proposal Cover Booklet. Take special care to see that the written and bubbled figures match exactly.

Below are the specific instructions for completing the Proposal Cover Booklet.

1. **Proposal Log Number.** (Leave blank.)
2. **Announcement Identifier.** Fill out with “OCR99-99” and proposal category selected from the list below (e.g., OCR99-99, Idea). The proposal category must be filled out with careful consideration because it will determine, in part, how your proposal will be assigned and evaluated for funding.

Proposal Category

Idea (Idea Award)
NIA (New Investigator Award)

3. **Proposal Category Code.** Select one of the codes listed below and enter it in the space provided. This must agree with the proposal category listed in question #2.

Proposal Category Category Code

Idea Award 01
New Investigator Award..... 02

4. **Organization Code.** (Leave blank.)

Appendix B

5. **Organization Name and Grants/Contracts Office Address.** Indicate the name and address of the organization that is submitting the proposal on the Principal Investigator's (PI's) behalf. This is the address for the Grants/Contracts/Business office of the PI's organization to enable us to contact the Administrative Representative listed in question #40 as the primary contact authorized to conduct negotiations on the PI's behalf.
6. **Type of Organization.** Choose one organization code that best describes your institution from the list below. Refer to the updated version of the list of the Department of Education recognized Historically Black Colleges and Universities/Minority Institutions (HBCU/MI) to determine HBCU/MI status. This list can be accessed on the CDMRP website at <http://cdmrp.army.mil>.

<u>Type of Organization</u>	<u>Organization Code</u>
Business-Large	A
Business-Small/Disadvantaged	B
Business-Small/Woman-Owned	C
Business-Small/Other.....	D
Educational Institution-HBCU	E
Educational Institution-MI	F
Educational Institution-Other	G
Federal Government-Air Force	H
Federal Government-Army	I
Federal Government-Navy	J
Federal Government-Veterans Affairs	K
Federal Government-DOD	L
Federal Government-Other.....	M
Foreign (non-U.S.)	N
Nonprofit	O
Other Organization.....	P
State Government.....	Q

7. **Principal Investigator Last Name, First Name, and Middle Initial.** The PI is the individual who is primarily responsible for the proposed research.
8. **Title.** Select the appropriate title for the PI.
9. **Principal Investigator's Degree.** Select all that apply.
- 10-17. **Principal Investigator's Mailing Address.** Fill in the PI's correct mailing address. This is the address where the work will be performed. **Do not use the PI's home address, and if possible, avoid the use of PO Boxes.** If applicable, indicate the PI's organization (question #10), department (question #11), then street address (questions #12 and #13). Do not use abbreviations or acronyms of any kind in the address. Do not use formal terms such as "The" or "The Trustees

Appendix B

of’ when indicating the organization. **When an organization or department name is not applicable, leave these sections blank, and then fill out the PI’s street, city, state, and zip code in the designated sections.** Applicants should use the appropriate country code listed below. International applicants should enter the international postal code in the space provided in question #17.

<u>Country</u>	<u>Code</u>	<u>Country</u>	<u>Code</u>	<u>Country</u>	<u>Code</u>
Argentina.....	AR	India.....	IN	Senegal	SN
Australia	AU	Indonesia	ID	Singapore.....	SG
Austria	AT	Ireland.....	IE	Slovakia.....	SL
Belgium	BE	Israel	IS	South Africa	ZU
Brazil	BR	Italy.....	IT	Spain.....	ES
Canada.....	CA	Jamaica	JM	Sri Lanka	CE
Chile	CL	Japan.....	JP	Sudan.....	SD
China	CN	Kenya.....	KE	Sweden	SE
Colombia.....	CO	Korea	KR	Switzerland.....	CH
Congo	CG	Korea, P.D.R.	KP	Taiwan.....	TW
Costa Rica	CR	Lebanon.....	LB	Thailand.....	TH
Czech Rep	CS	Malaysia	MY	Trinidad/Tobago...	TD
Denmark	DK	Mexico.....	MX	Turkey	TR
Egypt	EG	Netherlands.....	NL	Uganda	UG
Finland.....	FI	New Zealand.....	NZ	United Kingdom...	GB
France	FR	Norway	NO	United States	US
Germany	GY	Peru.....	PE	Uruguay	UY
Ghana	GH	Philippines.....	PH	Venezuela	VE
Greece.....	GR	Portugal	PT	Virgin Islands	VI
Guatemala.....	GT	Puerto Rico.....	RQ	West Africa	ZW
Iceland	IL	Russia	RU		

18-19. **Principal Investigator’s Phone and Fax Numbers.** U.S. phone and fax numbers must be filled in completely. International phone and fax numbers, including city code and country code, should be indicated in the spaces provided.

20. **Principal Investigator’s E-Mail Address.** If the PI has access to e-mail, write the address in the space provided.

21. **Principal Investigator Demographics.** (Optional.) Indicate the PI’s gender and ethnicity.

22. **Key Personnel Demographics.** (Optional.) Select all that apply for all of the key personnel.

Note: The data in questions #21 and #22 are being collected for demographic purposes and will be reported outside the Department of Defense only as grouped data without personal identifiers. Disclosure of this information is voluntary.

Appendix B

23. **Proposal Title.** Enter the title of the proposal, which may contain up to 160 characters. Capitalize the initial word and the first letter of each subsequent word, with the exception of prepositions and articles. Please count each blank space as equivalent to one character.
24. **Total Funding Requested from the Government.** Fill in the total dollar amount requested. This figure is inclusive of all direct and indirect costs for the entire period of the research as indicated in the Budget Section of the proposal. **Please be sure to include only the costs requested from the Government.** Do **NOT** include, in this figure, the amount the institution is willing to cost-share. Enter the amount in whole U.S. dollar figures only, and enter the numbers **FLUSH** with the right-hand margin.
25. **Military/Civilian Collaboration.** Indicate whether the proposal **DOES** or **DOES NOT** involve a military/civilian collaboration. If the proposal **DOES** represent a military/civilian collaboration, fill in the full name and address of the collaborating organization.
26. **Human Subjects.** Indicate whether the proposed research **DOES** or **DOES NOT** use human subjects. If yes, then select all that apply.
27. **Human Anatomical Substances.** Indicate whether the proposed work **DOES** or **DOES NOT** use human anatomical substances. If yes, then select all that apply.
28. **Clinical Trials.** Indicate whether the proposed work **DOES** or **DOES NOT** involve clinical trials. If yes, then select all that apply.
29. **Demographics of Human Test Subjects/Study Population of Interest.** If human subjects are being used, you **MUST** complete this entire section. If human subjects are **NOT** being used, then select **NOT APPLICABLE**.
30. **Animal Subjects.** Indicate if the proposed work **DOES** or **DOES NOT** use animal subjects. If yes, then select all that apply.
31. **Safety Provisions.** Select all that apply.
32. **Mentor Name.** (Leave blank.)
33. **Research Classification.** (Leave blank.)
34. **Research Area Level 1.** Select **ONE** primary Research Area Code that best describes the proposed research from the CDMRP Research Classification on page B-6.
35. **Research Area Level 2.** Select **ONE** secondary Research Area Code that best describes the proposed research from the CDMRP Research Classification on page B-6. If no other code applies, please code 0000.

Appendix B

36. **Research Area Level 3.** Select **ONE** primary Research Area Code that best describes the proposed research from the National Cancer Institute/Department of Defense Common Scientific Outline on page B-12.
37. **Research Area Level 4.** Select **ONE** secondary Research Area Code that best describes the proposed research from the National Cancer Institute/Department of Defense Common Scientific Outline on page B-12. If no other code applies, please code 0000.
38. **Research Area Level 5.** (Leave blank.)
39. **Other Proposal Submission in a Different Proposal Category.** (Leave blank.)
40. **Administrative Representative Authorized to Conduct Negotiations.** Indicate the primary and secondary administrative contacts authorized to conduct negotiations on the PI's behalf. The address for the primary contact must be indicated in question #5 on the first page of the Proposal Cover Booklet. If the organization has a Grants/Contracts/Business Official, this is the individual authorized to negotiate potential awards. The signature of the institutional representative certifies that the institution has examined the PI's credentials and verifies that the PI is qualified to conduct the proposed study and to use humans or animals as research subjects, if appropriate. **THIS SIGNATURE IS MANDATORY.**
41. **Institution's Official Proposal Control Number.** This is the number that the institution uses to track your proposal. This number, if available, should be provided by the institution's Grants/Contracts/Business office listed in questions #5 and #40.
42. **Principal Investigator.** The PI must fill out this information and sign in the space indicated. **THIS SIGNATURE IS MANDATORY.**

CDMRP Research Classification
(used for questions 34 and 35)

Cell Biology: Covers the study of the cell, its structure, including cellular organization, regulation, composition, and function of normal and transformed cells.

- 0101 Cell cycle: Sequence and regulation of cellular events between mitotic divisions.
- 0102 Cell surface proteins: Proteins that are involved in mediating the recognition and adhesion of cells to their substrates and to other cells to include adhesion, matrix, and membrane bound proteins.
- 0103 Growth factors/cytokines/signaling: Intercellular signaling polypeptides and their receptors (which control the ontogeny and maintenance of tissue form and function) and the activation of the intracellular pathways.
- 0104 Oncogenes: Genes whose mutation promotes tumor development/malignant phenotype.
- 0105 Tumor suppressor gene: Genes whose mutation or overexpression promotes tumor development/malignant phenotype.
- 0199 Not otherwise specified: Cell biology not otherwise specified in the other research areas.

Molecular Biology and Genetics: Covers studies on the molecular structures and events underlying biological processes, especially the relation between genes and the functional characteristics they determine.

- 0201 Chromosome structure: Organization of the DNA into a chromosome, the accompanying chromosomal elements, and staining and sequencing techniques.
- 0202 DNA damage and repair: Enzymatic correction of errors in DNA structure and sequence that result from replication errors.
- 0203 Genomic instability: Genetic changes that result in new combinations of alleles and/or chromosomal modifications such as crossing over, deletions, and translocations.
- 0204 Familial and hereditary carcinogenesis: Genes and their products that cause initiation, progression, and spread of cancer in familial or hereditary clusters.
- 0205 Transcription, translation and modification: Process by which genetic information encoded in a gene is converted into RNA and protein and subsequent post-translational modifications.
- 0299 Not otherwise specified: Molecular biology and genetics not otherwise specified in other research areas.

Endocrinology: Covers studies on structure and function of endocrine glands, their products, and their control to include hormones and their receptors.

- 0301 Clinical endocrinology: Hormonal functions, ligand interactions, and metabolism as it relates to bedside and clinical applications.

Appendix B

- 0302 Endocrine carcinogenesis: Role of hormones in the initiation and support of cancer growth.
- 0303 Hormone metabolism: Biosynthesis, degradation, and enzymatic interconversions of hormones and structural analogs.
- 0304 Hormone receptors: Membrane-bound or intracellular molecules that bind with high affinity to, or respond to, hormones.
- 0305 Mechanism of hormone action: Ligand and its receptor interaction on targeted metabolic processes and the downstream consequences of this interaction.
- 0399 Not otherwise specified: Endocrinology not otherwise specified in the other research areas.

Pathobiology: Covers studies on the pathological cell and tissue specifically related to cancer to include cellular structure, organization, regulation, composition, and function.

- 0401 Angiogenesis: Neo-vascularization associated with tumor growth and the proteins and genes that mediate this phenomenon.
- 0402 Apoptosis: Process of a particular form of cell death, programmed cell death, which is characterized by specific morphologic and biochemical properties.
- 0403 Biomarkers: Cellular constituents whose presence and/or concentration might serve as an indicator of the predisposition, presence, or progression of cancer.
- 0404 Environmental carcinogenesis: Influence and/or linkage of chemicals and other environmental pollutants with high risks of specific types of cancer.
- 0405 Progression/invasion/metastasis: Cell proliferation from the time of initial transformation to metastasis.
- 0406 Stromal epithelial interactions: Role of the interaction of the stromal and epithelial elements of the cell in the initiation of cancer.
- 0499 Not otherwise specified: Pathobiology not otherwise specified in the other research areas.

Immunology: Covers studies on the response of the organism to antigenic challenge, and the cell mediated and humoral aspects of immunity and immune responses.

- 0501 Molecular: Looking beyond the cell to identify immune markers and characterize antibody structures as well as genetic engineering and progressive cloning.
- 0502 Tumor: Interaction between tumors and the immune system, including anti-tumor immune responses and recognition of tumor antigens.
- 0503 Psychoneuroimmunology: Effect of psychological stressors on immune responses.

Appendix B

0504 Immunopathology: Contributions of immune system disruption to tumor development and progression.

0599 Not otherwise specified: Immunology not otherwise specified in the other research areas.

Prevention: Covers studies on the prevention of cancer occurrence.

0601 Lifestyle: Contributions and consequences of lifestyle and behavioral factors on cancer risk, prognosis, treatment and/or rehabilitation; also studies that test lifestyle interventions to reduce cancer and/or rehabilitation requirements. Lifestyle factors in this category would include, for example, exercise and diet.

0602 Chemoprevention: Effect(s) of drugs to prevent the occurrence of cancer.

0603 Nutrition: Contributions and consequences of diet and/or nutrition on cancer risk; also test diet and/or nutrition interventions to prevent the occurrence of cancer.

0699 Not otherwise specified: Prevention not otherwise specified in the other research areas.

Detection and Diagnosis: Covers studies of improved detection and diagnostic techniques.

0701 Biomarkers: Use of compounds detectable in blood, body fluids, or tissues, whose detection can be used for screening or diagnosis.

0702 Cell/tissue sampling: Methods for collecting cell or tissue samples and the most effective testing of these samples for the detection or diagnosis of disease.

0703 Computer-aided diagnosis: Computer programs and artificial intelligence systems to assist in the evaluation of radiographic or other diagnostic information.

0704 Digital imaging: Capturing, storing, viewing, and analyzing radiographic or other images in a digital format.

0705 Magnetic resonance imaging: Visualization of structures in the body by use of oscillating magnetic fields and analysis of the resulting radio frequencies produced.

0706 Position emission tomography scan: Tissue function imaging using positron-emitting isotopes and emission-computed tomography.

0707 Ultrasonography: Visualization of structures in the body by recording the reflections of high frequency sound waves directed into the tissues.

0708 X-ray imaging/computed tomography: Visualization of structures in the body by ionizing radiation.

0709 Other imaging: Imaging modalities not otherwise specified in the other research areas.

0799 Not otherwise specified: Diagnostic modalities not otherwise specified in the other research areas.

Appendix B

Clinical and Experimental Therapeutics: Covers studies on clinical and therapeutic agents to assess their use in treatment.

- 0801 Cytotoxic chemotherapy: Use of drugs or a combination of drugs to kill cancer cells.
- 0802 Drug discovery/development: Screening and testing of potential new agents, modification of existing agents, and study of new routes of administration for existing agents.
- 0803 Drug resistance/multi-drug resistance (MDR): Mechanisms, treatments, and prevention of classical MDR and other forms of drug resistance.
- 0804 Targeted therapies (conjugated toxins): Development, testing, and study of chimeric compounds that combine a targeting component with a toxic or therapeutic component.
- 0805 Nutraceuticals: Vitamins and dietary supplements as treatments.
- 0806 Immunotherapies: Treatment of disease by either passive or active immunization or by the use of agents designed to potentiate or suppress actions of lymphocytes.
- 0807 Radiotherapy: Use of high-energy rays (e.g., x-rays) to kill cancer cells or halt their growth. Includes external and implant radiation sources.
- 0808 Hormonal therapy: Cancer treatment by removing, blocking, or adding hormones.
- 0809 Gene therapy (includes vector development): Treatment that inserts normal or genetically altered genes into cells in order to improve the body's natural ability to fight disease or to make the tumor more sensitive to other therapies.
- 0810 Combined therapies: Cancer treatment that uses a combination of therapy modalities.
- 0811 Anti-angiogenics: Use of substances that inhibit blood vessel formation accompanying malignant tumor growth.
- 0812 Surgery: Procedures designed to remove or repair tissue cells.
- 0813 Hyperthermia: Localized or systemic temperature increases for either direct therapeutic effect or enhancing the effectiveness of other therapies.
- 0899 Not otherwise specified: Clinical and experimental therapeutics not otherwise specified in the other research areas.

Alternative Medicine: Covers studies of treatments and health care practices and/or applications of treatments and practices that are not taught widely in health care curricula, not generally used in hospitals, and not usually reimbursed by medical insurance companies.

- 0901 Nutrition, vitamins, and dietary supplements: Nutritional, vitamin, and/or dietary supplements and/or applications of nutritional, vitamin, and/or dietary supplements that are not taught widely in health care curricula, not generally used in hospitals, and not usually reimbursed by medical insurance companies.

Appendix B

0999 Not otherwise specified: Application of non-nutritional, vitamin, and/or dietary supplement treatments and practices that are not taught widely in health care curricula, not generally used in hospitals, and not usually reimbursed by medical insurance companies.

Health Care Delivery: Covers studies assessing the delivery of cancer prevention, detection, treatment, and rehabilitation services.

1001 Systems: Describing and assessing existing systems and/or policies for the delivery of cancer prevention, detection, treatment, and rehabilitation services.

1002 Interventions: Assessment of interventions and/or potential new policies designed to improve the delivery of cancer prevention, detection, treatment, and rehabilitation services.

1099 Not otherwise specified: Health care delivery not otherwise specified in the other research areas.

Behavioral and Psychosocial Sciences: Covers studies of the relationship(s) between behavioral and social functioning and cancer prevention, initiation, progression, control, treatment, and rehabilitation.

1101 Basic behavioral: Basic relationships between biobehavioral or behavioral factors (e.g., knowledge, attitudes, and behavior) and cancer.

1102 Pain and pain management: Behavioral and social factors to cancer pain and/or to the relief from or control of pain associated with cancer and/or cancer treatment and rehabilitation.

1103 Quality of life: Behavioral and social factors affecting the lives of cancer patients (including cancer risk, diagnosis, treatment and/or rehabilitation); also test behavioral and social interventions aimed at improving the quality of cancer patients' lives.

1104 Decision-making: Behavioral and social factors that contribute to, or the behavioral and social consequences that result from, decisions by patients, caregivers, and providers concerning cancer risk, diagnosis, treatment and/or rehabilitation; also test behavioral and social interventions to enhance decision-making.

1105 Outreach and inreach: Behavioral and social factors that influence, and/or to identify and test interventions for reaching target populations in communities (outreach) or medical settings (inreach) with cancer information and/or services.

1199 Not otherwise specified: Behavioral and psychosocial sciences not otherwise specified in the other research areas.

Appendix B

Epidemiology: Covers population- and patient-based observational research studies of the distribution of cancer as well as the behavioral and/or biological determinants of cancer risk, cancer initiation and/or progression, cancer detection, and cancer prognosis.

- 1201 Surveillance: Population- and patient-based observational research studies of the distribution of cancer in defined populations.
- 1202 Behavioral epidemiology: Population- and patient-based observational studies assessing the nature of associations between behavioral factors and cancer risk, cancer initiation and/or progression, cancer detection, and cancer prognosis and treatment.
- 1203 Molecular epidemiology: Population- and patient-based observational studies assessing the nature of associations between molecular and/or genetic markers and cancer risk, initiation and/or progression, cancer detection, cancer prognosis, and/or known behavioral risk factors for cancer.
- 1204 Environmental epidemiology: Population- and patient-based observational studies assessing the nature of associations between environmental factors and/or exposures and cancer risk, initiation and/or progression, cancer detection, and cancer prognosis.
- 1299 Not otherwise specified: Epidemiological studies not otherwise specified in the other research areas.

Research Resources: Covers support for the development and/or maintenance of institutional, regional, or national facilities to sustain biomedical research.

- 1301 Cancer training program: Support for extramural programs to train investigators.
- 1302 Tissue and serum banks: Support for studies and for the development and maintenance of repositories for the storage and distribution of tissue, plasma, and other biological material.
- 1303 Animal models: Support for development of animal models of human diseases.
- 1304 Computer models: Support for the development and maintenance of computer modeling and information management systems.
- 1305 Cancer centers: Support for the development of core-supported, multi-project research programs integrated around a common theme.
- 1306 Statistical models: Support for the development of models for data analysis.
- 1307 Databases: Support for the development, expansion, and/or maintenance of integrated, large-scale data collections.
- 1399 Not otherwise specified: Research resources not otherwise specified in the other research areas.

National Cancer Institute/Department of Defense Common Scientific Outline
(used for questions 36 and 37)

Biology

- 1100 Biology including developmental biology: Biology of the organism, organs, tissues, cells, and subcellular organelles. Developmental biology from conception to adulthood and the biology of aging. Study of normal functioning genes, their localization, identification, expression patterns, and functional studies of gene products. Extracellular matrix formation and interactions, cell-cell interactions; and cell signaling pathways.
- 1200 Initiation; progression; metastasis; regression: Initiation, including general mechanisms of carcinogen metabolism and DNA damage, DNA repair pathways, mutation fixation, clone selection, clone development; epigenetic mechanisms. Progression, including clonal evolution, immune interactions; factors which influence clonal expansion or regression, and tumor promotion. Metastasis, including studies involving cell-cell interaction, tumor-host interactions, cell motility, remodeling of cellular matrix, cell migration, and clonal expansion at distant sites. Regression.
- 1300 Resources and infrastructure related to biology: Education and training of investigators. Informatics and informatics networks, for example, patient databanks. Specimen resources (tissue, serum, etc.). Reagents, chemical standards, and pharmaceuticals.

Etiology

- 2100 Exogenous factors: Lifestyle factors such as smoking, chewing tobacco, alcohol consumption, parity, diet, and exercise. Environmental and occupational exposures such as second-hand smoke, radon, asbestos, organic vapors, pesticides, and other chemicals. Infectious agents such as Human Papilloma Virus (HPV).
- 2200 Endogenous factors: Hormones and growth factors; oxygen and other free radicals. Genes known to be involved or suspected of being mechanistically involved in familial cancer syndromes, for example, BRCA1 and APC. Genes suspected or known to be involved in “sporadic” cancer events, for example, polymorphisms and/or mutations that may affect carcinogen metabolism (e.g., CYP, NAT). Tumor suppressor genes (e.g., p53) and oncogenes (e.g., RAS).
- 2300 Interactions of genes and/or genetic polymorphisms with exogenous and/or endogenous factors: Gene-environment interactions. Interactions of genes with lifestyle factors, environmental and/or occupational exposures. For example, variations in carcinogen metabolism associated with genetic polymorphisms. Interactions of genes and endogenous factors such as DNA repair deficiencies and endogenous DNA damaging agents such as oxygen radicals.
- 2400 Resources and infrastructure related to etiology: Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, etc.). Reagents, chemical standards, pharmaceuticals. Epidemiological study methods. Statistical methodology or biostatistical methods.

Appendix B

Prevention

- 3100 Interventions to prevent cancer: Personal behaviors that affect cancer risk: Research on determinants of personal behaviors, such as diet, physical activity, sun exposure and tobacco use, that affect cancer risk. Interventions to change behavior to reduce cancer risk.
- 3200 Nutritional science in cancer prevention: Qualifications of nutrients and micronutrients. Studies on the effect(s) of nutrients or nutritional status on cancer incidence. Dietary assessment efforts including dietary questionnaires and surveys. Development, characterization, and validation of dietary/nutritional assessment instruments.
- 3300 Chemoprevention: Chemopreventive agents and their discovery, development, testing in model systems, and clinical testing preventives.
- 3400 Resources and infrastructure related to prevention: Education and training of investigators. Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, etc.). Epidemiological (observational) studies. Clinical trials. Statistical methodology or biostatistical methods.

Early Detection, Diagnosis, and Prognosis

- 4100 Technology development and/or marker discovery: Discovery of markers (e.g., proteins, genes) and/or imaging methods that are potential candidates for use in cancer detection, diagnosis, and/or prognosis.
- 4200 Technology and/or marker evaluation with respect to fundamental parameters of method: Preliminary evaluation with respect to laboratory sensitivity, laboratory specificity, reproducibility, and accuracy.
- 4300 Technology and/or marker testing in a clinical setting: Evaluation of clinical sensitivity, clinical specificity, and predictive value. Quality assurance and quality control. Inter- and intra-laboratory reproducibility. Testing of the method with respect to effects on morbidity and/or mortality. Study of screening methods including compliance, acceptability to potential screenees, receiver-operator characteristics.
- 4400 Resources and infrastructure related to detection, diagnosis, or prognosis: Education and training of investigators. Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, etc.). Clinical trials. Epidemiological studies pertaining to risk assessment, detection, diagnosis or prognosis. Statistical methodology or biostatistical methods.

Treatment

- 5100 Localized therapies: Discovery, development, and testing of treatments that target the organ and/or neighboring tissue directly, for example, surgical interventions and radiotherapy.
- 5200 Systemic therapies: Discovery, development and testing of cytotoxic or hormonal therapies that are given systemically to the organism or individual. Discovery, development, and testing of novel systemic therapies such as immunologically directed therapies (vaccines, antibodies), gene therapy, angiogenesis inhibitors, apoptosis inhibitors, and differentiating agents. Treatment.
- 5300 Combinations of localized and systemic therapies: Discovery, development, and testing of combined approaches to treatment such as chemo/hormonal therapy with gene therapy, adjuvant therapy, antiangiogenesis inhibitors, or immunologically based therapies

Appendix B

5400 Resources and infrastructure related to treatment: Education and training of investigators. Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, etc.). Mathematical and computer simulations. Clinical trial groups. Statistical methodology or biostatistical methods. Drugs and reagents for distribution.

Cancer Control, Survivorship, and Outcomes Research

6100 Survivorship issues (post-treatment concerns): Quality of life – post-treatment. Pain management – post-treatment. Psychological impacts of cancer survivorship. Rehabilitation. Reproductive issues. Long-term morbidity.

6200 Patient care (diagnosis through treatment) including supportive: Quality of life – diagnosis through treatment. Pain management – diagnosis through treatment. Symptom management including nausea, vomiting, lymphedema, neuropathies, etc. Prevention of treatment-related toxicities and sequelae including symptom management, prevention of mucosities, prevention of cardiotoxicities, etc.

6300 Surveillance: Epidemiology and End Results Reporting (SEER). Surveillance of cancer risk factors such as diet, body weight, physical activity, sun exposure, tobacco use. Analysis of variations in risk factor exposure by demographic or other factors. Registries that track incidence, morbidity, and/or mortality related to cancer. Trends in use of interventional strategies. Method development for risk factor surveillance.

6400 Behavior related to cancer control: Behavior medicine research and interventions. Influence of social factors, such as, community, policy, education, and legislation, on behaviors related to cancer control. Attitudes and belief systems and their influence on psychological health and on behaviors related to cancer control, for example, how beliefs can alter attempts to seek screening, detection, and treatment. Interventions to change attitudes and beliefs that affect behavior related to cancer control and cancer outcomes. Influences of attitudes and beliefs on compliance to treatment and prevention protocols. Psychological or educational interventions to promote behaviors that lessen treatment-related morbidity and promote psychological adjustment to the diagnosis of cancer and to treatment effects. Burdens of cancer on family members and psychological/behavior issues.

6500 Cost analyses and health care delivery: Analyses of cost-effectiveness of methods used in cancer prevention, detection, diagnosis, prognosis, and survivor care/support. Studies of providers such as geographical or care-setting variations in outcomes. Affect of reimbursement and/or insurance on cancer control, outcomes, and survivorship support. Access to care issues.

6600 Education and communication: Development of communication tools and methods. Education of patients, physicians, at-risk populations and general population about cancer. Communication to patients regarding therapeutic options. Educational interventions to promote self-care and symptom management. Communicating cancer risk to underserved populations, at-risk populations, and the general public. Alternative teaching methods to communicate therapeutic options and risk education behavior to patients or the general public. Communication of life style models that reduce cancer risk; nutrition interventions. Communicating smoking and tobacco cessation interventions. Special approaches and considerations for underserved and at-risk populations. Education, information, prevention/screening/assessment systems for the general public or primary care professionals. Training, predictive cancer models, pain management, and surveillance systems for primary care professionals; telehealth/telemedicine applications. Communication regarding cancer genetics; managed oncology care; survivorship issues. Barriers to successful health communication.

Appendix B

- 6700 End of life care: End of life care issues including palliative care, psychological interventions with families at end of life, hospice care, pain management for terminally ill patients, etc.
- 6800 Ethics and confidentiality in cancer research: Informed consent modeling and development. Quality of IRBs. Protecting patient confidentiality and privacy. Research ethics.
- 6900 Resources and infrastructure related to cancer control, survivorship, and outcomes research: Education and training of investigators. Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, etc.). Clinical trial groups. Statistical methodology or biostatistical methods.

Complementary and Alternative Approaches

- 7100 Prevention approaches: Discovery and testing of natural and synthetic substances, use of psychologic, behavioral, or interventional approaches not used in conventional medicine or applied in different ways.
- 7200 Treatment approaches: Discovery and testing of natural substances, use of psychologic, behavioral, or interventional approaches not used in conventional medicine or applied in different ways.
- 7300 Supportive approaches: Hypnotherapy, relaxation, transcendental meditation, imagery, spiritual healing, massage, biofeedback.
- 7400 Resources and infrastructure related to complementary and alternative approaches: Education and training of investigators. Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, etc.). Clinical trials. Statistical methodology or biostatistical methods.

Scientific Model Systems

- 8100 Development of model systems: Development of model systems, including computer-simulation model systems, *in vitro* models systems, cell culture model systems, organ and tissue model systems, and animal model systems such as *drosophila* and *C. elegans*.
- 8200 Characterization of model systems: Characterization of model systems, including, computer-simulation model systems, *in vitro* models systems, cell culture model systems, organ and tissue model systems, and animal model systems such as *drosophila* and *C. elegans*.
- 8300 Resources and infrastructure related to scientific model systems: Models made available for distribution to the scientific community.

Unable to Code

- 9100 Unable to code – Please review: Those abstracts that you are unable to identify a reasonable fit and wish to have reviewed.

Appendix C

Proposal Preparation

Appendix C of this Announcement contains specific instructions for proposal preparation.

Table of Contents

<u>Part</u>	<u>Page</u>
1. Who May Apply	C-2
2. Proposal Acceptance Criteria	C-3
3. Proposal Cover Booklet (Bubble Sheet)	C-4
4. Peer Review Referral Page.....	C-4
5. Proposal Title Page.....	C-5
6. Table of Contents	C-5
7. Proposal Abstracts.....	C-5
8. Statement of Work	C-6
9. Proposal Relevance and Impact Statement	C-6
10. Proposal Body	C-7
11. References	C-7
12. Biographical Sketches	C-7
13. Existing/Pending Support.....	C-7
14. Facilities/Equipment Description.....	C-7
15. Support Documentation.....	C-8
16. Detailed Cost Estimate	C-8
17. Instruments	C-8
18. Publications and Patent Abstracts	C-8
19. Proposal Submission	C-8
20. Submission Deadline.....	C-9
21. Appendices	C-10
22. Notification.....	C-10

Proposal Preparation

1. Who May Apply

Eligible institutions include for-profit and nonprofit organizations, public and private, such as universities, colleges, hospitals, laboratories, companies, and agencies of local, state, and federal governments, including military laboratories. Any individual, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by or affiliated with an eligible institution. The U.S. Army Medical Research and Materiel Command (USAMRMC) is especially interested in receiving applications from Historically Black Colleges and Universities/Minority Institutions (HBCU/MIs).

Investigators are cautioned that awards are made to institutions. Should the Principal Investigator (PI) of a funded project leave the recipient institution, both the PI and an official of the recipient institution should contact the U.S. Army Medical Research Acquisition Activity (USAMRAA) awarding office prior to the PI leaving the recipient institution to discuss any options available for continued support of the research project.

Historically Black Colleges and Universities/Minority Institutions

The goal of the DOD is to allocate a targeted percentage (5.5%) of total funds for the Congressionally Directed Medical Research Programs' (CDMRP's) peer reviewed research to fund proposals from HBCU/MIs. These funds are intended to "advance the development of human potential, to strengthen the capacity of Historically Black Colleges and Universities to provide quality education, and to increase opportunities to participate in and benefit from Federal programs."¹ Similar guidance has also been provided for Minority Institutions in other Executive Orders.² An institution's HBCU/MI status is based upon whether it is recognized as a U.S. Department of Education (DOEd) HBCU/MI on the date the Announcement for this program was released. The DOEd HBCU/MI list will be used to verify institutional HBCU/MI status. An updated DOEd list is posted on the CDMRP website (<http://cdmrp.army.mil>, select HBCU/MI List and refer to the program to which you are applying). Any individual, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by or affiliated with an eligible institution.

HBCU/MI proposals will be reviewed concurrently with all others in the same research area during scientific peer review, but may be evaluated separately during programmatic review when award recommendations are determined. Consistent with the CDMRP's goal, the final investment strategy for HBCU/MI funds will be based upon scientific excellence and program relevance.

¹ Executive Order 12876.

² Executive Orders 12900 and 13021.

2. Proposal Acceptance Criteria

Compliance guidelines have been designed to present the proposal in an organized and easy-to-follow manner to scientific reviewers responsible for reviewing its merit. Scientific merit reviewers will expect to see a consistent, prescribed format for each reviewed proposal. Non-adherence to format requirements (such as font size, margins, and line spacing) makes proposals difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in proposal rejection or a poorer priority score in peer review. In particular, the review of applications containing more than the allotted number of pages will be restricted to the pages within the page limitations (excess pages *will* be removed), and **excess pages will not be forwarded for peer review.**

It is required that the instructions in this section be followed carefully. The application shall be clear, legible, and conform to the following format, spacing, font size, margins, and printing guidelines:

- **PIs are strongly encouraged to spell out all acronyms the first time they are used.**
- Language: English.
- Margins: Minimum of 0.5 inch top, bottom, right, and left.
- Paper Size: 8.5 x 11.0 inches. (Note to international applicants: A4 paper will be accepted if the text of the proposal does not exceed 7.5 x 10.0 inches [approximately 19 cm x 25.5 cm].)
- Printing: Single-sided. (Double-sided printed pages are not accepted, with the exception of article reprints.)
- Spacing: Single-spaced between lines of text, no more than 5 lines of type within a vertical inch.
- Type Color: Black ink including all graphs, diagrams, tables, and charts. The application should contain only material that can be photocopied. Submitting investigators should be cautioned that if color graphs or photographs are included, they may not reproduce in subsequent photocopies. Therefore, submission of color figures, tables, graphs, or photographs is not recommended and is at the investigator's own risk.
- Type Density: No more than 15 characters per inch. (For proportional spacing, the average for any representative section of text should not exceed either 15 characters per inch or 114 characters per line.)
- Type Font: 12 point, 10 pitch, no more than 15 characters per inch and 114 characters per line.

Appendix C

To assist applicants, the following example is included.

This illustrates the minimum font size and margins, and the required line spacing. This illustrates the minimum font size and margins, and the required line spacing. This illustrates the minimum font size and margins, and the required line spacing. This illustrates the minimum font size and margins, and the required line spacing. This illustrates the minimum font size and margins, and the required line spacing.

****Important Note Regarding Amended Proposals****

Re-submissions of previously reviewed proposals are acceptable. However, the applicant should be cautioned that the year-to-year status of funding for the Ovarian Cancer Research Program (OCRP) does not permit the establishment of standing panels for peer review. Therefore, the re-submission of a revised proposal does not guarantee any funding advantage or an improved priority score. Re-submitted/amended proposals should meet the requirements for the appropriate award category in the current Announcement and adhere to this year's format guidelines.

3. Proposal Cover Booklet (Bubble Sheet)

Complete this form as described in Appendix B, Proposal Cover Booklet Instructions.

1. Each proposal should include 1 original plus 3 photocopies of the Proposal Cover Booklet.
2. Proposal Cover Booklets can be requested via fax, phone, e-mail, or mail at the addresses/numbers in the Foreword. Please allow sufficient time for delivery by regular mail.

4. Peer Review Referral Page – Start section on a new page – No page limit

The Peer Review Referral Page shall contain the following sections:

1. Proposal Title.
2. PI's Full Name, including middle initial.
3. Keyword Descriptive Technical Terms. Every effort is made to assign proposals to an appropriate peer review panel. First, specify which research focus area (e.g., cancer biology, prevention, detection, diagnosis, and/or therapy) will be addressed. Then, list specific keywords and descriptive technical terms that would best describe the technical

Appendix C

aspects of the project (e.g., cell signaling, apoptosis, angiogenesis, drug delivery systems, gene therapy, x-ray crystallography, genetic counseling, quality of life, nuclear medicine, immunology, clinical oncology, and nutrition).

4. Conflicts of Interest. Every effort is made to avoid real and apparent conflicts of interest during the peer review process. In order to assist the staff in this regard, list the names of all scientific participants in the proposal including the PI, co-investigators, research associates, research assistants, consultants, collaborators, and subcontractors. Provide the following information for each participant: name, degree(s), scientific discipline or medical specialty (e.g., radiology, immunology, clinical oncology, nutrition, pathology, cell biology, and endocrinology), institutional affiliation(s), title(s), and role(s) on proposed project.

5. Proposal Title Page – Start section on a new page – 1 page limit

The Proposal Title Page should include the following information:

1. Proposal Title
2. Award Mechanism
3. PI's full name, including middle initial
4. PI's phone number, fax number, and e-mail address
5. Organization name and location (including city, state, zip or postal code, and country)
6. Contracting Representative's name
7. Contracting Representative's phone number, fax number, and e-mail address
8. Proposed start date

6. Table of Contents – Start section on a new page – 1 page limit

Prepare a Table of Contents, with page numbers, using the outline provided in the Proposal Preparation section under each award mechanism. As listed, number all pages of the sections consecutively at the bottom center, beginning with the Proposal Title Page.

7. Proposal Abstracts – Start each abstract on a new page – 2 page limit

The abstracts are vitally important to the review of the proposal. Both a 1 page maximum technical abstract and a 1 page maximum public (non-technical) abstract are required. Each proposal abstract page should contain the title of the proposal and the name of the PI. The technical abstract should provide a clear and concise overview of the proposed work including the hypothesis and its supporting rationale, the objectives and specific aims of the study, the rationale for the hypotheses, the research design, the study methods, and the relevance of the proposed work to the program's goals. The public abstract is intended to communicate the purpose of and rationale for the study to the non-scientific community. It should be composed in a way to make the scientific objectives of and rationale for the proposal understandable to non-scientifically trained readers. **Programmatic review is based upon the Integration Panel's**

review of these two abstracts as part of the peer review summary statements; therefore, it is paramount that the investigator submit abstracts that fully describe the proposed work. Do not include figures in either abstract.

In addition to the abstract pages contained within the proposal, submit 5 copies of each of the abstracts in a manila envelope, along with a 3½" computer disk containing the abstracts (clearly labeled with the name of the PI, institution, and word processing program). It is recommended that abstracts be written in WordPerfect, Word, or ASCII format. [Note: Abstracts of all funded proposals will be reproduced in an abstract book and posted on the CDMRP website (<http://cdmrp.army.mil>). Thus, proprietary information should not be included in the abstract].

8. Statement of Work – Start section on a new page – 2 page limit

The Statement of Work is a concise re-statement of the research proposal that outlines and establishes the PI performance expectations and timeline for which the USAMRMC will provide financial support. Although some allowance is made for encountering problems and uncertainties that are a part of research, the PI is expected to meet the provisions and milestones of the Statement of Work.

The Statement of Work should be a series of relatively short statements that outline, step-by-step, how each of the major goals or objectives of the proposed research will be accomplished. As appropriate, the Statement of Work should:

1. describe the work to be accomplished as tasks (may relate tasks to specific aims),
2. identify the timeline and milestones for the work over the period of the proposed effort,
3. indicate the numbers of research subjects (animal or human) for each task,
4. identify methods, and
5. identify products/deliverables for each phase of the project.

As a guide, the Statement of Work for a 3-year effort should require approximately 1 page of single-spaced typing. Several sample Statements of Work are included as a reference in Appendix D of this Program Announcement.

9. Proposal Relevance and Impact Statement – Start section on a new page – 1 page limit

In the Proposal Relevance and Impact Statement, the investigator should describe how the proposed research is pertinent to one or more critical issues of the disease.

10. Proposal Body – Start section on a new page – 10 page limit

Each award mechanism has specific instructions for the description of the project. Investigators should refer to the specific evaluation criteria listed under the award mechanism to which they are applying to ensure that the necessary information is included.

Use black ink for all graphs, diagrams, tables, and charts. The application should contain only material that can be photocopied. Submitting investigators should be cautioned that if color graphs or photographs are included, they may not reproduce in subsequent photocopies. Therefore, submission of color figures, tables, graphs, or photographs is not recommended and is at the investigator's own risk.

11. References – No page limit

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).

12. Biographical Sketches – 3 page limit per investigator

Biographical sketches should be prepared for each of the key personnel listed on the budget page including collaborating investigators and mentors. Biographical sketches may not exceed 3 pages. The "Biographical Sketch" form can be found in Appendix E, or it can be downloaded from the CDMRP website (<http://cdmrp.army.mil>). A list of significant publications and a succinct summary of the investigator's professional experience in the disease and/or their potential for contribution to the field should be incorporated into the biographical sketch.

13. Existing/Pending Support – No page limit

List on a separate page, the titles, time commitments, supporting agencies, durations, and levels of funding for all existing and pending research projects involving the PI and key personnel. Proposals submitted under this Announcement should not duplicate other funded research projects. If no support exists, state 'none'.

14. Facilities/Equipment Description – No page limit

Describe the facilities available for performance of the proposed research. Describe the institutional commitment including any additional facilities or equipment proposed for acquisition or available for use at no cost to the USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use.

15. Support Documentation – No page limit

Provide letter(s) from proposed collaborating individuals or institutions confirming collaborative efforts that are necessary for the project's success. Note that other support documentation also may be required within specific award categories. Please follow specific instructions in each award mechanism. *This section is not for additional data, figures, or other similar information.*

16. Detailed Cost Estimate – No page limit

Use the Detailed Cost Estimate form to prepare a detailed cost estimate of the proposed research. This form can be found in Appendix F, or it can be downloaded from the CDMRP website (<http://cdmrp.army.mil>). The cost of preparing proposals in response to this Program Announcement is not considered an allowable direct charge to any resultant award.

17. Instruments – No page limit

Attach questionnaires, survey instruments, or clinical protocols as they apply to the proposal.

18. Publications and Patent Abstracts – 5 document limit

You may include up to five relevant publication reprints and patent abstracts. A patent abstract should provide a non-proprietary description of the patent application. If more than five such items are included in the submission, **the extra items will not be forwarded to peer review.**

19. Proposal Submission

Submit the following documentation to the address listed in the Foreword under Proposal Submission:

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.

Proposal Cover Booklet: **ONE** original (binder-clipped to the original proposal) and **THREE** photocopies (*not* binder-clipped to proposal copies).

Letters of Recommendation: If required, binder-clipped to the front of original proposal under the original Proposal Cover Booklet. See individual application instructions.

Appendix C

Abstract Pages: An additional **FIVE** copies of both the technical and the public (non-technical) abstracts in a manila envelope along with a 3½" computer disk containing the abstract pages (clearly labeled with the name of the PI, institution, and word processing program). It is recommended that abstracts be formatted in Word, WordPerfect, or ASCII.

Note: The abstracts are *vital* to the review of the proposal. Abstracts of all funded proposals will be reproduced in an OCRP abstract book and posted on the CDMRP website (<http://cdmrp.army.mil>).

Packaging: Package only **ONE** complete proposal submission (original plus all copies requested above) per box. If acknowledgment of proposal receipt is desired, enclose a self-addressed, stamped postcard with each submission. This postcard should state the proposal title and PI's name.

Send the Proposal to: The address listed in the Foreword, part 1 for Proposal Submission.

20. Submission Deadline

The submission deadline for all awards solicited in this Announcement is listed in the Foreword and under each award mechanism.

Any proposal received by the USAMRMC after the exact time specified for receipt shall **not** be considered unless it is received before award is made, and:

1. it was sent by mail, and it is determined by the Government that late receipt was due solely to mishandling by the Government after receipt at the Government installation, or
2. it was sent by U.S. Postal Service Express Mail Next Day Delivery (Post Office to Addressee: **Do not use Second Day Delivery**) and postmarked no later than 8:00 p.m. (local time at point of origination) the day before the proposal receipt deadline, or
3. it was placed into the control of a commercial courier service no later than 8:00 p.m. (local time at point of origination) the day before the proposal receipt deadline for delivery by 4:00 p.m. Eastern Time on the due date, or
4. the Government, in its sole discretion, decides to accept the late proposal if it determines that no competitive advantage has been conferred, and the integrity of the competitive grants process will not be compromised.

Appendix C

Investigators are advised that documentation of time of receipt by the delivery agent may be necessary if a problem should occur.

21. Appendices – To be submitted at a later date

Appendices G (Certificate of Environmental Compliance), H (Research Involving Human Subjects and/or Anatomical Substances), I (Research Involving Animals), and J (Safety Program Plan) outline Regulatory Compliance and Quality (RCQ) requirements. Appendix K (Representations and Certifications for Grants and Cooperative Agreements) outline USAMRAA requirements. This information should be provided by the PI to the USAMRMC immediately upon request but *should not be submitted with the original proposal*.

22. Notification

Following completion of the two-tiered evaluation process, every applicant will receive a letter indicating their funding status, along with a scientific summary critique of their proposal. Scientific review summaries will contain the criteria scores, the global score, and detailed comments that address the proposal's strengths and weaknesses with respect to each evaluation criterion. Notification letters will be sent as official information is available. Thus, not all investigators will be notified at the same time.

Appendix D

Sample Statements of Work

JONES, R.E.

Statement of Work

Development of Peptide Inhibitors of the “Cancer” Receptor (CR)

- Task 1.* To identify the minimal region of the CR polypeptide able to inhibit intact CR when co-expressed in cultured cells (months 1-18):
- a. develop a series of plasmids for expressing the CR open reading frame (months 1-7)
 - b. perform assays to ascertain which fragments of CR block deoxyribonucleic acid (DNA)-binding (months 7-18)
 - c. confirm that fragments of the CR open reading frame that block DNA-binding activity also inhibit CR function *in vivo* (months 18-24)
- Task 2.* To identify short peptides modeled after the receptor that act as inhibitors of DNA binding and subunit association (months 18-36):
- a. obtain synthetic CR peptides (months 18-21)
 - b. test the effect of synthetic peptides on the DNA-binding activity of CR (months 20-24)
 - c. characterize the inhibitory potency of active peptides and attempt to optimize the effect by testing additional overlapping peptides (months 21-36)
 - d. perform feasibility experiments to assess the ability of selected peptides to inhibit CR function in cultured cells (months 20-36)

Statement of Work

Follow-up Care for Women with Ovarian Cancer

- Task 1.* Develop Plan for Follow-up Patient Interviews, Months 1-3:
- a. The tracking system shell from the previous ovarian cancer project will be modified to track patient recruitment and contact process.
 - b. The follow-up patient interview will be pre-screened with ovarian cancer patients from our hospital who are not enrolled in our study and modifications will be incorporated.
 - c. The environmental process interview (EPI) used for the baseline interview will be adapted for the follow-up interview.
 - d. Institutional Review Board approval will be obtained from all hospital sites.
 - e. The patient interviewer will be trained in medical terminology, measures of the interview, and use of the modified EPI system.
- Task 2.* Preparation for Medical Record Abstractions, Months 3-9:
- a. The Medical Record Abstract form will be finalized and the investigator trained to perform patient data reviews using the instrument.
 - b. The Medical Record Abstract form will be revised for direct computer data entry.
- Task 3.* Subject Recruitment and Data Collection, Months 9-20:
- a. Patients enrolled in our previous study will be recruited for the proposed follow-up study.
 - b. Interviews subsequent to the first follow-up will be modified as necessary to reflect issues relevant to patients beyond the period of adjuvant therapy.
 - c. Surveys will be sent to and data collected from enrolled patients every 6 months.
- Task 4.* Abstraction of Medical Records, Months 12-24:
- a. Medical record abstractions will be performed for surviving enrolled patients annually.
 - b. Data entry and quality control measures will be ongoing.
 - c. Follow-up interviews will be conducted once annually with surviving enrolled patients over the 4-year period.
- Task 5.* Interim Analyses, Months 24-44:
- a. Interim statistical analyses of data obtained from interviews and medical record abstractions will be performed periodically.
 - b. Annual reports will be written.

Appendix D

- Task 6.* Final analyses and report writing, Months 44-48:
- a. Final analyses of data from interviews and medical record abstractions will be performed.
 - b. A final report and initial manuscripts will be prepared.

Appendix E

Biographical Sketches

Provide the following information for the key personnel listed on the budget page for the initial budget period.			
NAME		POSITION TITLE	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include post-doctoral training.)			
INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
<p>RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds 2 pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.</p>			

Appendix E

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY.
DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Appendix E

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY.
DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Appendix F

Detailed Cost Estimate Instructions

The following sections describe the categories of costs that should be recorded in the detailed cost estimates using the standard budget sheets. All amounts entered should be in U.S. dollars.

Table of Contents

<u>Part</u>	<u>Page</u>
1. Personnel	F-2
2. Consultant Costs.....	F-3
3. Major Equipment.....	F-3
4. Materials, Supplies, and Consumables.....	F-3
5. Travel Costs.....	F-3
6. Research-Related Patient Costs.....	F-3
7. Other Expenses.....	F-4
8. Consortium Costs	F-4
9. Indirect Costs.....	F-4
10. Budget for Entire Proposed Period of Support.....	F-4
11. Budget Justification.....	F-5

1. Personnel

Show projected salary amounts in terms of annual salary and percentage of effort on the project to be charged by the Principal Investigator (PI), co-investigator(s), research associate(s), and assistant(s), and the total amount per year to be paid to each staff member of the project. Starting with the PI, list the names of all employees of the applicant who will be involved in the project during the initial budget period, regardless of whether salaries are requested. Include all collaborating investigators, individuals in training, and support staff. Only **ONE** person may be identified as the PI of the proposal.

The qualifications of the PI and the amount of time that he/she and other senior professional key personnel will devote to the research are important factors affecting the selection of research proposals for funding. Awards may be terminated when the PI severs connections with the organization or is unable to continue active participation in the research. Investigators are cautioned that awards are made to institutions. Should the PI of a funded project leave the recipient institution, both the PI and an official of the recipient institution should notify the U.S. Army Medical Research Acquisition Activity (USAMRAA) prior to leaving the recipient institution to discuss any options available for continued support of the research project.

- **Role on Project:** Identify the role of each individual listed on the project. Describe their specific functions in the *Justification* (page 3 of the Detailed Cost Estimate form).
- **Type of Appointment (Months):** List the number of months per year reflected in an individual's contractual appointment with the offering organization. DOD staff assume that appointments at the applicant organization are full time for each individual. If an appointment is less than full time, e.g., 50 percent time, note this with an asterisk (*) and provide a full explanation in the *Justification* (page 3 of the budget form). Individuals may have split appointments (e.g., for an academic period and a summer period). For each appointment, identify and enter the number of months on separate lines.
- **Annual Base Salary:** Enter the annual institutional base salary for each individual listed for the project.
- **Percentage of Effort on Project:** For each key staff member identified on the budget form, list the percentage of each appointment to be spent on this project.
- **Salary Requested:** Enter the salaries in whole dollar figures for each position for which funds are requested. The salary requested is calculated by multiplying an individual's institutional base salary by the percentage of effort on the project.

Appendix F

- **Fringe Benefits:** Fringe benefits may be requested in accordance with institutional guidelines for each position, provided the costs are treated consistently by the applicant organization as a direct cost to all sponsors. A copy of the rate agreement or other documentation to support the fringe benefits should be provided.
- **Totals:** Calculate the totals for each position and enter these as subtotals in the columns indicated.

2. Consultant Costs

Regardless of whether funds are requested, provide the names and organizational affiliations of all consultants, other than those involved in consortium arrangements.

3. Major Equipment

It is the policy of the DOD that all commercial and nonprofit recipients provide the equipment needed to support proposed research. In those rare cases where specific additional equipment is approved for commercial and nonprofit organizations, such approved cost elements shall be separately negotiated.

4. Materials, Supplies, and Consumables

A general description and total estimated cost of expendable equipment and supplies are required. Itemize supplies in separate categories (e.g., glassware, chemicals, and radioisotopes). Categories in amounts less than \$1,000 do not need to be itemized. If animals are to be purchased, state the species and the number to be used.

5. Travel Costs

List the number of trips, destinations, and purposes for all proposed travel. Estimate round-trip travel fare and per diem costs for each trip. Travel to scientific meetings requires identification of the meeting and purpose. No more than one trip to a scientific meeting per award per year is funded. Itemize travel requests and justify time in the *Justification* (page 3 of the budget form).

6. Research-Related Patient Costs

Itemize costs of patient participation in the research study. These costs are strictly limited to expenses specifically associated with the proposed study. The USAMRMC will not provide funds for ongoing medical care costs that are not related to a subject's participation in the research study.

7. Other Expenses

Itemize other anticipated direct costs such as publication and report costs, rental for computers and other equipment (giving hours and rates), and communication costs. Unusual or expensive items should be fully explained and justified. Estimate the costs of publishing and reporting research results, including direct charges for clerical preparation, illustrations, reprints, and distribution.

8. Consortium Costs

A description of services or materials that are to be awarded by subcontract or subgrant is required. For awards totaling \$10,000 or more, provide the following specific information:

- a. the identification of the type of award to be used (e.g., cost reimbursement and fixed price);
- b. if known, the identification of the proposed subcontractor or subgrantee and an explanation of why and how the subcontractor or subgrantee was selected or will be selected;
- c. whether the award will be competitive and, if noncompetitive, rationale to justify the absence of competition; and
- d. the proposed acquisition price.

9. Indirect Costs (overhead, general and administrative, and other)

The most recent rates, dates of negotiation, base(s), and periods to which the rates apply should be disclosed along with a statement identifying whether the proposed rates are provisional or fixed. A copy of the negotiation memorandum should be provided.

Training awards frequently have a different institutional overhead charge. All training investigators are encouraged to check with their institution concerning overhead costs.

10. Budget for Entire Proposed Period of Support (second budget page)

Enter the totals under each budget category for all additional years of support requested and itemize these totals in the *Justification* (on page 3 of the budget form). **Note with an asterisk (*) and explain any significant increases or decreases from the initial year budget. Also, explain any escalations of the budget from the initial to the future year(s) of support.** All amounts should be in U.S. dollars. Total costs for the entire proposed period of support on the last line of this page should agree with the amount entered in #24 of the Proposal Cover Booklet (Bubble Sheet).

11. Budget Justification (third budget page)

Each item in the budget should be clearly justified under *Justification* (on page 3 of the budget form). In addition, for projects with a substantial foreign component, explain and justify this on the *Justification* page.

Detailed Cost Estimate Form

Principal Investigator (*last, first, middle*)

DETAILED BUDGET FOR INITIAL BUDGET PERIOD					FROM	THROUGH	
PERSONNEL		TYPE APPT. (MONTHS)	ANNUAL BASE SALARY	% EFFORT ON PROJECT	DOLLAR AMOUNT REQUESTED (OMIT CENTS)		
NAME	ROLE ON PROJECT				SALARY REQUESTED	FRINGE BENEFITS	TOTALS
	Principal Investigator						
SUBTOTALS →→→→→							\$
CONSULTANT COSTS							
MAJOR EQUIPMENT (ITEMIZE)							
MATERIALS, SUPPLIES, AND CONSUMABLES (ITEMIZE BY CATEGORY)							
TRAVEL COSTS							
RESEARCH-RELATED PATIENT COSTS							
OTHER EXPENSES (ITEMIZE BY CATEGORY)							
SUBTOTAL OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD →→→→→							\$
CONSORTIUM COSTS	DIRECT COST						
	INDIRECT COST						
TOTAL PERSONNEL & OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD							\$
TOTAL INDIRECT COSTS FOR INITIAL BUDGET PERIOD							\$
TOTAL COSTS FOR INITIAL BUDGET PERIOD							\$

Appendix F

Principal Investigator (*last, first, middle*)

BUDGET FOR ENTIRE PROPOSED PERIOD OF SUPPORT						
BUDGET CATEGORY TOTALS*	INITIAL BUDGET PERIOD <small>(FROM FORM PAGE 1)</small>	ADDITIONAL YEARS OF SUPPORT REQUESTED				TOTAL
		2nd	3rd	4th	5th	
PERSONNEL						
FRINGE BENEFITS						
CONSULTANT COSTS						
MAJOR EQUIPMENT						
MATERIALS, SUPPLIES, AND CONSUMABLES						
TRAVEL COSTS						
RESEARCH-RELATED PATIENT COSTS						
OTHER EXPENSES						
SUBTOTAL DIRECT COSTS						
CONSORTIUM COSTS	DIRECT					
	INDIRECT					
TOTAL DIRECT COSTS						
TOTAL INDIRECT COSTS						
TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PERIOD OF SUPPORT					\$	
TOTAL INDIRECT COSTS FOR ENTIRE PROPOSED PERIOD OF SUPPORT					\$	
TOTAL COSTS FOR THE ENTIRE PROPOSED PERIOD OF SUPPORT THIS AMOUNT SHOULD AGREE WITH THAT ENTERED ON THE PROPOSAL COVER BOOKLET, ITEM #24					\$	

* Itemize all budget categories for additional years on *Justification* page that follows.

Appendix F

JUSTIFICATION: FOLLOW THE BUDGET JUSTIFICATION INSTRUCTIONS EXACTLY. USE CONTINUATION PAGES AS NEEDED.

Appendix G

Certificate of Environmental Compliance

The Certificate of Environmental Compliance should be executed by the institution's official responsible for environmental compliance.

The Council on Environmental Quality (CEQ) regulations (40 CFR 1500-1508) that implement the National Environmental Policy Act (NEPA) (PL 91-190, as amended) require all federal agencies to examine possible environmental consequences of their proposed and ongoing actions.

The U.S. Army Medical Research and Materiel Command (USAMRMC) examines all medical research and development projects, whether inside or outside the United States, for their potential environmental impacts. In most cases, awardees conducting research in established laboratories that are in compliance with environmental laws and regulations, or are already covered by existing environmental documentation, will not be required to provide additional information about the environmental impact of their proposed research. Such projects will receive a "categorical exclusion" according to the Army regulations that implement the CEQ regulations (AR 200-2). After a proposal has been selected for award, the USAMRMC will determine if a categorical exclusion is warranted. If there are any extraordinary circumstances surrounding the research [e.g., research that involves the transfer of recombinant deoxyribonucleic acid (DNA) molecules into the genome of one or more human subjects, requires Biosafety Levels 3 and 4, or uses animals captured from the wild], further information may be requested from the investigator to determine the environmental impact of the proposed research. This information should be submitted in a timely manner in order to receive an award.

Appendix H

Research Involving Human Subjects and/or Human Anatomical Substances

Appendix H of this Announcement contains the required approvals, forms, and descriptions for research involving human subjects and/or human anatomical substances (including human organs, tissues, cells, body fluids from human subjects as well as graphic, written, or recorded information derived from human subjects). Address all issues relating to the use of human subjects and anatomical substances in the proposed research.

Note that Department of Defense (DOD) rules for participation of subjects and informed consent differ from those required by other funding agencies.

Table of Contents

<u>Part</u>	<u>Page</u>
1. Introduction	H-3
2. Definitions	H-3
2-a. Research	H-3
2-b. Human Subjects.....	H-3
3. Human Subjects Research Review Board Process.....	H-4
3-a. Review Levels	H-4
3-b. Timelines and Outcomes.....	H-4
4. Claim of Exempt Research.....	H-5
4-a. Exempt Research Involving Human Subjects or Anatomical Substances	H-5
4-b. Exempt Categories	H-5
4-c. Claiming Exemption	H-6
4-d. Final Judgment	H-6
5. Guidelines for Writing Research Protocols Involving Human Subjects.....	H-7
5-a. The Basic Protocol	H-7
5-b. Requirements Unique to DOD/USAMRMC-Funded Research.....	H-9
5-b.i. Reporting of Serious and Unexpected Adverse Events.....	H-9
5-b.ii. Volunteer Registry Database.....	H-9
5-b.iii. Sample Donation.....	H-10
5-b.iv. Participation of Subjects.....	H-10
5-b.v. Medical Monitor.....	H-10
5-b.vi. Pregnancy Testing	H-11
5-b.vii. Research-Related Injury Costs	H-11
5-c. Advertisements, Posters, Flyers, or Press Releases to Recruit Subjects	H-11
5-d. Surveys, Questionnaires, or Other Instruments	H-12

Table of Contents (Cont.)

<u>Part</u>	<u>Page</u>
5-e. Investigational Drugs or Devices	H-12
6. Informed Consent Requirements	H-12
6-a. Elements of Informed Consent.....	H-12
6-b. Additional Elements of Informed Consent.....	H-13
6-c. Requirements Unique to DOD/USAMRMC-Funded Research.....	H-14
6-c.i. Certification of Translation	H-14
6-c.ii. Payment for Study Participation: Active Duty Military Personnel	H-14
6-c.iii. Confidentiality: Military Personnel.....	H-14
6-c.iv. Pregnant Women	H-14
6-c.v. Volunteer Registry Database	H-14
6-d. Documentation of Informed Consent	H-15
7. Assurances	H-15
8. Inclusion of Women and Minorities in Research.....	H-15
9. Where to Go for Help and Information	H-15
10. Claim of Exemption from Review by the Human Subjects Research Review Board.....	H-17
Optional Form 310	H-18

Research Involving Human Subjects and/or Anatomical Substances

1. Introduction

In 1991, the DOD, along with 15 other federal agencies, adopted regulations that are known collectively as the Common Federal Rule. These regulations embody the ethical principles of the Belmont Report. Title 32, Code of Federal Regulations, Part 219 (32 CFR 219), “Protection of Human Subjects” applies to all research involving human subjects conducted or supported by the DOD. The Department of Health and Human Services (DHHS) National Institutes of Health (NIH) corollary is 45 CFR 46. Research conducted or funded by the U.S. Army Medical Research and Materiel Command (USAMRMC) is also governed by Army Regulation (AR) 70-25, January 1990 and Office of The Army Surgeon General (OTSG) Regulation 15-2, January 1989. The USAMRMC also adheres to the Food and Drug Administration’s (FDA’s) regulation, Title 21, Code of Federal Regulations for research involving investigational drugs or devices.

The OTSG maintains the overall responsibility for protecting human research subjects for the Department of the Army (DA).

2. Definitions

2-a. Research

32 CFR 219, The Common Federal Rule, defines “research as a systematic investigation, including research development, testing, and evaluation designed to develop or contribute to generalizable knowledge.” Activities that meet this definition constitute research for purposes of this policy, whether they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities.

21 CFR 312 (FDA) defines “clinical investigation” as “any experiment that involves a test article and one or more human subjects.”

2-b. Human Subjects

32 CFR 219 defines “human subject” as “a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information.” **The regulations extend to the use of human organs, tissues, cells, body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects.**

21 CFR 312 (FDA) defines “human subject” as “an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.”

3. Human Subjects Research Review Board Process

3-a. Review Levels

In addition to the first level of review and approval by the local Institutional Review Board (IRB), the OTSG requires a second level of review and approval by its Human Subjects Research Review Board (HSRRB) of all research involving human subjects. See Section 2-b of this appendix for the definition of a human subject. ***Approval must be obtained prior to initiation of the research protocol.***

The HSRRB is functionally similar to a civilian IRB. The HSRRB is supported administratively by the staff of the Office of the Deputy Chief of Staff for Regulatory Compliance and Quality (ODCSRCQ), Human Subjects Protection Division (HSPD), USAMRMC.

If the research proposal is recommended for funding and the research involves human subjects, the HSRRB, in accordance with 32 CFR 219, will determine that the research:

1. is exempt from HSRRB review,
2. is eligible for expedited review,
3. is no greater than minimal risk and, therefore, may be administratively reviewed and approved by the Acting Chair, HSRRB, or
4. is greater than minimal risk and, therefore, requires full HSRRB committee review.

3-b. Timelines and Outcomes

In general, research protocols that pose greater than minimal risk to subjects are submitted through the ODCSRCQ to the HSRRB for full committee review and approval prior to implementation of the study. Review and approval by the HSRRB are usually accomplished within 45-90 days after submission of the protocol to the HSRRB. Any revisions to the protocol, consent form(s), advertisements, questionnaires, and other related study documentation recommended by the HSRRB must be reviewed and approved by the Acting Chair, HSRRB **prior to implementation of the study.**

The HSRRB will make one of the following recommendations to The Surgeon General (TSG):

1. approval of proposal without changes,
2. conditional approval of proposal contingent upon changes and/or clarification,

3. deferred (Note: Protocols are deferred when the HSRRB has substantive concerns about the conduct of the protocol or the safety of the subjects. The Principal Investigator (PI) will receive written comments from the HSRRB and the investigator's responses will go to full committee for further deliberation.), or
4. disapproved (Note: The PI will be notified of this decision in writing. The PI must then notify the ODCSRCQ of his/her intention to re-submit the protocol or to terminate consideration of the protocol.).

4. Claim of Exempt Research

4-a. Exempt Research Involving Human Subjects or Anatomical Substances

Certain categories of research may be exempt from review by the HSRRB. Those categories are specific and follow federal guidelines. An investigator's research must fit into one or more of the categories in order to file the Claim of Exemption form.

4-b. Exempt Categories

The following list details the exemption categories.

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
 - A. research on regular and special education instructional strategies, or
 - B. research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless:
 - A. information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
 - B. any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph 2 of this section, if:
 - A. the human subjects are elected or appointed public officials or candidates for public office; or

Appendix H

- B. federal statute(s) requires without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- 4. Research involving the collection or study of existing data, documents, records, or pathological or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- 5. Research and demonstration projects that are conducted by or subject to the approval of Department or Agency heads, and that are designed to study, evaluate, or otherwise examine:
 - A. public benefit or service programs,
 - B. procedures for obtaining benefits or services under those programs,
 - C. possible changes in or alternatives to those programs or procedures, or
 - D. possible changes in methods or levels of payment for benefits or services under those programs.
- 6. Taste and food quality evaluation and consumer acceptance studies:
 - A. if wholesome foods without additives are consumed, or
 - B. if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

4-c. Claiming Exemption

Complete the form in Section 10 of this appendix to claim exemption for research involving human subjects or anatomical substances (organs, tissues, cells, or body fluids). Consult with the IRB office staff for institutional policies and procedures for exempt research.

4-d. Final Judgment

The HSRRB retains final judgment as to whether a particular activity is covered by this policy.

5. Guidelines for Writing Research Protocols Involving Human Subjects

5-a. The Basic Protocol

A detailed research protocol is required for the HSRRB review of your research. All submissions should include the following information:

1. **Project Title.** The consent form title should match that of the project.
2. **Phase.** For Food, Drug, and Cosmetic Act-regulated medical products, designate as a Phase I, II, III, or IV protocol.
3. **Principal Investigator.** The complete name, address, and phone number of the PI should be listed.
4. **Location of Study.** List all centers, clinics, or laboratories where the study is to be carried out. The complete addresses and site investigator(s) should be listed.
5. **Time Required to Complete.** The month and year of expected start and completion should be listed.
6. **Objectives.**
7. **Study Population.** Detail source, number, age range, and sex of subjects along with inclusion/exclusion criteria.
8. **Protocol Design.** Outline the proposed methodology in enough detail to show a clear course of action. Technological reliability and validity of procedures should be indicated. Minimum guidance for the plan includes:
 - A. Subject identification (Describe code system to be used.)
 - B. Subject assignment
 - C. Evaluations prior to entry
 - D. Evaluations to be made during the conduct of the study (e.g., laboratory evaluations, specimens to be collected, schedule and amounts, storage to include where and whether special conditions are required, labeling and disposition)
 - E. Clinical Assessments (e.g., schedule of clinical evaluations and follow-up procedures, and adverse events)
9. **Risks/Benefits Assessment.** (Detail benefits of the research to the subject, precautions to be taken to minimize and/or eliminate risks, and specific medical or nursing care that will be needed.)
10. **Reporting of Serious and Unexpected Adverse Events.** (See HSRRB Clause 1.02-

Section 5-b.i. of this appendix)

11. **Description of Protocol Drug(s) or Device(s).** If the protocol uses an investigational drug or device, provide the following information:
 - A. Investigational New Drug (IND)/Investigational Device Exemption (IDE) number and sponsor
 - B. Complete names and composition of all medication(s), device(s), or placebo(s)
 - C. Source of medication(s), device(s), placebo(s)
 - D. Place where study medication(s) will be stored
 - E. Dose range, schedule, and administration
 - F. Washout period (The washout or pre-drug period must be noted carefully.)
 - G. Duration of drug or device treatment
 - H. Concomitant medications
 - I. Antidotes and treatments available
 - J. Disposition of unused drug

12. **Disposition of Data.** Describe where the data will be stored and for how long.

Note: Records for IND studies must be kept until 2 years after a New Drug Application (NDA)/license for the investigational drug is approved/issued, or for 2 years after the IND is withdrawn. Records required for IDE studies should be retained for 2 years after the later of the following dates: the date that investigation is terminated or completed; or the date that records are no longer required for support of a premarket approval application.

13. **Modification of the Protocol.** Describe the procedure to be followed if the protocol is modified.

14. **Roles and Responsibilities of Study Personnel.** Briefly describe the duties of study personnel.

15. **Signature of Principal Investigator.** Type the following statement, “I have read the foregoing protocol and agree to conduct the study as outlined herein.” The PI should sign and date following this statement.

5-b. Requirements Unique to DOD/USAMRMC-Funded Research

5-b.i. Reporting of Serious and Unexpected Adverse Events

HSRRB Clause 1.02

Serious and unexpected adverse experiences will be immediately reported by telephone to the USAMRMC Deputy Chief of Staff for Regulatory Compliance and Quality [(301) 619-2165, during non-duty hours call (301) 619-2165 **and** send information by fax to (301) 619-7803]. A written report will follow the initial telephone call within 3 working days. Address the written report to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RCQ-HR, 504 Scott Street, Fort Detrick, MD 21702-5012.

HSRRB Clause 7.01

An adverse event temporally related to participation in the study should be documented whether considered to be related to the test article. This definition includes intercurrent illnesses and injuries, and exacerbations of pre-existing conditions. Include the following in all IND safety reports: Subject identification number and initials; investigator's name and name of hospital or medical treatment facility; subject's date of birth, gender, and ethnicity; test article and dates of administration; signs/symptoms and severity; date of onset; date of resolution or death; relationship to the study drug; action taken; concomitant medication(s) including dose, route and duration of treatment, and date of last dose.

5-b.ii. Volunteer Registry Database

HSRRB Clause 2.01

It is the policy of the USAMRMC that data sheets are to be completed on all volunteers participating in research for entry into this Command's Volunteer Registry Database. The information to be entered into this confidential database includes name, address, social security number, study name, and dates. The intent of the database is twofold: first, to readily answer questions concerning an individual's participation in research sponsored by USAMRMC; and second, to ensure that the USAMRMC can exercise its obligation to ensure research volunteers are adequately warned (duty to warn) of risks and to provide new information as it becomes available. The information will be stored at USAMRMC for a minimum of 75 years.

5-b.iii. Sample Donation

HSRRB Clause 4.01

If the samples donated in this study will be used in other studies, the statement “I understand that there is a possibility that the blood, tissue, body fluid, product, or sample(s) (specify type) which I am providing under this study may also be used in other research studies and could potentially have some commercial applicability” should be included in the consent form. In addition, a donation form must be prepared for signature by the volunteer and a witness that states “I voluntarily and freely donate any and all blood, tissues, body fluid, product, or sample(s) (specify type) to the study sponsor (insert institution name) and hereby relinquish all right, title, and interest to said items.” The title of the study should be inserted at the top of this donation form. The samples that will be stored should contain no personal identifiers.

5-b.iv. Participation of Subjects

HSRRB Clause 6.01

10 United States Code 980 requires that “Funds appropriated to the Department of Defense may not be used for research involving a human being as an experimental subject unless (1) the informed consent of the subject is obtained in advance; or (2) in the case of research intended to be beneficial to the subject, the informed consent may be obtained from a legal representative of the subject.”

Furthermore and consistent with the Common Federal Policy for the Protection of Human Subjects, if an individual cannot give his or her own consent to participate in a research study, consent of the individual’s legally authorized representative must be obtained prior to the individual’s participation in the research. Moreover, an individual not legally competent to consent (e.g., incapacitated individuals, incompetents, minors) may not be enrolled in DOD-funded research unless the research is intended to benefit each subject enrolled in the study. For example, a subject may benefit directly from medical treatment or surveillance beyond the standard of care. Proposers should be aware that this law makes placebo controlled clinical trials problematic because of the ‘intent to benefit’ requirement whenever participation is sought of subjects from whom consent must be obtained by the legally authorized representative.

5-b.v. Medical Monitor

HSRRB Clause 8.01

A medical monitor must be assigned to any study involving greater than minimal risk to subjects. The name and curriculum vitae of the medical monitor must be provided. This individual should be a qualified physician, other than the PI, not associated with this particular protocol, able to provide medical care to research subjects for conditions that

may arise during the conduct of the study, and who will monitor the subjects during the conduct of the study.

5-b.vi. Pregnancy Testing

If pregnant subjects will be excluded from participation in the study, the **method of determining pregnancy** status in women of childbearing potential must be specified. Also, the time that will elapse between the pregnancy test and exposure to research procedures or medical products must be documented. Pregnancy tests are required for all clinical medical product studies. For IND studies, serum or urine pregnancy testing is required within 48 hours prior to the start of the study.

5-b.vii. Research-Related Injury Costs

For research involving greater than minimal risk, include the following explanation of medical care available for research-related injury (HSRRB Clause 3.01):

Should you be injured as a direct result of participating in this research project, you will be provided medical care, at no cost to you, for that injury. You will not receive any injury compensation, only medical care. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the principal investigator before you enroll in this study.

Three possible mechanisms are available to offset the costs of this requirement:

1. The proposed recipient may absorb such costs into the institution's operating budget.
2. The proposed recipient's liability insurance, if available, may be sufficient to cover any medical care costs. The proposed recipient's business office and/or legal advisor must ensure that there is adequate coverage under this liability insurance.
3. The proposed recipient could negotiate an additional amount of funds, if available, into the award that will cover such medical care cost (such as liability insurance).

5-c. Advertisements, Posters, Flyers, or Press Releases to Recruit Subjects

If subjects will be recruited through an advertisement, newspaper article, or similar process, a copy of the local IRB-approved advertisement must be provided. For studies involving investigational drugs or devices, local IRB review of advertisements is necessary to ensure the information is not misleading to the subjects participating in IND or IDE studies. The FDA has established guidelines on advertisements for subjects. General guidance includes: name and address of PI, summary of research purpose, brief eligibility criteria, truthful list of benefits, and the person to contact for further information.

5-d. Surveys, Questionnaires, or Other Instruments

If the research involves surveys, questionnaires, or other instruments, include copies of the instruments.

5-e. Investigational Drugs or Devices

For research that involves an investigational drug or device:

1. Submit a copy of the Investigator's Drug Brochure and/or device manual and associated case report/data collection forms.
2. For IND products, specify the IND number, name of the sponsor, and the procedure by which the IND sponsor will monitor the protocol in accordance with 21 CFR 312.
3. For Investigational Devices, include your local IRB's assessment of the risk of the investigational device you plan to use in your study. If the device poses significant risk to research subjects, specify the IDE number obtained from the FDA, the name of the sponsor, and the procedure by which the IDE sponsor will monitor the protocol in accordance with 21 CFR 812.
4. Contact your local IRB and/or the FDA if you have questions regarding IND or IDE submission requirements.

6. Informed Consent Requirements

The information that is given to the subject or his/her representative shall be in language understandable to the subject or the representative. No informed consent may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

6-a. Elements of Informed Consent

The following information is essential for informed consent documents:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental.
2. A description of any reasonably foreseeable risks or discomforts to the subject.

Appendix H

3. A description of any benefits to the subject or to others that may reasonably be expected from the research.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
6. The name of the investigator as a point of contact for answers to questions about the research and research subjects' rights, and the name of the IRB contact in the event of a research-related injury to the subject.
7. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

6-b. Additional Elements of Informed Consent

When appropriate, one or more of the following elements of information shall also be provided to each subject:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable.
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
3. Any additional costs to the subject that may result from participation in the research.
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
5. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.
6. The approximate number of subjects involved in the study.

6-c. Requirements Unique to DOD/USAMRMC-Funded Research

6-c.i. Certification of Translation

HSRRB Clause 5.01

Provide documentation that the foreign language version of the consent form is an accurate translation. Documentation should include the following statement, “I certify that this is an accurate and true translation” as well as the signature, name, address, phone number and, if available, fax number of the translator.

6-c.ii. Payment for Study Participation: Active Duty Military Personnel

Under 24 CFR 30, payment for participation is limited to blood donation and may not exceed \$50 per blood draw. Active duty research subjects may not receive any other payment for participation in a research study.

6-c.iii. Confidentiality: Military Personnel

The following statement is **MANDATORY** for studies utilizing military personnel:

All data and medical information obtained about you as an individual will be considered privileged and held in confidence; you will not be identified in any presentation of the results. Complete confidentiality cannot be promised, particularly to subjects who are military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities.

6-c.iv. Pregnant Women

If pregnant women will be excluded, the following statement, HSRRB Clause 9.01 (or equivalent), must be included:

You should avoid becoming pregnant for at least (time period in days, weeks, or months) after participation in the study. To avoid becoming pregnant, you should either abstain from sexual relations or practice a method of birth control. Except for surgical removal of the uterus, birth control methods such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm-killing products are not totally effective in preventing pregnancy.

6-c.v. Volunteer Registry Database

For all studies involving greater than minimal risk, HSRRB Clause 2.01, Volunteer Registry Database, must be included in the consent form. See Section 5-b.ii. of this appendix.

6-d. Documentation of Informed Consent

The following information is required: (1) a signature block for the subject or from the legal, authorized representative; (2) a permanent address for the subject; and (3) a signature block, including the printed name, of the witness.

7. Assurances

If an institution has filed a Multiple Project Assurance (MPA) with the DHHS Office for Protection from Research Risks (OPRR), that assurance number should be documented on the Optional Form 310 (OF 310, Protection of Human Subjects Assurance/Certification/Declaration, page G-19), which replaced DHHS Form 596.

If the institution has not filed an MPA with OPRR, a written Assurance of Compliance should be filed with the USAMRMC Office of the Deputy Chief of Staff for Regulatory Compliance and Quality, Human Subjects Protection Division. A DOD Assurance number will be issued for the research project. There are three different assurance applications: (1) for institutions that have an IRB but no MPA; (2) for overseas institutions; and (3) for institutions using another institution's IRB. Sample assurance documents and the OF 310 can be downloaded from the USAMRMC Congressionally Directed Medical Research Programs website (<http://cdmrp.army.mil>).

The OF 310 should be completed and signed by the Chairperson of the IRB. If another agent signs this document, verification of authority should be included in the remarks column (individual's signature authority). The OF 310 **must** include the level of risk that the project poses to the subject. These risk levels are: exempt, no more than minimal risk, and greater than minimal risk. The HSPD reserves the right to determine whether the assigned risk level is in compliance with all applicable regulations.

8. Inclusion of Women and Minorities in Research

Consistent with the Belmont Report and recent Congressional legislation, special attention is given to inclusion of women and minorities in research funded by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. If women and/or minorities will be excluded, a justification must be included.

9. Where to Go for Help and Information

If your research involves human subjects, you should first contact your local IRB for institutional requirements.

Appendix H

If you have questions regarding the USAMRMC protocol and consent form requirements or the review and approval process, contact the Office of the Deputy Chief of Staff for Regulatory Compliance and Quality at the address, phone number, or e-mail address listed below:

Phone: (301) 619-2165
E-mail: yvonne.higgins@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-RCQ-HR
504 Scott Street
Fort Detrick, MD 21702-5012

References:

- Title 32 Code of Federal Regulations, Part 219, Protection of Human Subjects
- Title 21 Code of Federal Regulations, Part 50, Protection of Human Subjects
- Title 21 Code of Federal Regulations, Part 56, Institutional Review Boards
- Title 21 Code of Federal Regulations, Part 312, Investigational New Drug Application
- Title 21 Code of Federal Regulations, Part 812, Investigational Devices
- Army Regulation 70-25, Use of Volunteers as Research Subjects
- Army Regulation 40-7, Use of Investigational Drugs and Devices in Humans and the Use of Schedule I Controlled Drug Substances
- Office of The Surgeon General Regulation 15-2, Human Subjects Research Review Board
- Title 45 Code of Federal Regulations, Part 46 (45 CFR 46), Subparts B, C, and D, Protection of Human Subjects
- Title 10 United States Code, Section 980
- Department of Defense Directive 3216.2
- Department of Defense Directive 6465.2 (when using organs or tissues obtained at autopsy)

10. Claim of Exemption from Review by the Human Subjects Research Review Board

United States Army Medical Research and Materiel Command
Office of the Deputy Chief of Staff for Regulatory Compliance and Quality
Human Subjects Protection Division

PROTOCOL TITLE
INVESTIGATOR'S NAME
INSTITUTION

EXEMPT CATEGORY CLAIMED (Please refer to Exempt Categories - Section 4-b.)

1. Will existing or archived data, documents, medical records, or database records be used? Yes No
2. Will biological specimens (i.e., cells, tissues, blood) be used? Yes No
3. Indicate below the source(s) of existing or archived data/biological specimens or cell lines (e.g., cells purchased from ATCC).

4. Will the information be recorded in such a manner that subjects cannot be identified, directly or indirectly, through links? Yes No
5. Will data be recorded in writing? Yes No
6. Will data be recorded by an audiotape? Yes No
7. Will data be recorded by videotape? Yes No
8. If survey instruments are used, will sensitive or private topics be explored? Yes No
9. Will the subjects be identifiable either by name or through demographic data? If yes, describe on a separate sheet how the confidentiality of a subject's identity will be maintained and plans for maintaining or destroying identifying links to subjects after the study is completed. Yes No

PI's Signature

**Protection of Human Subjects
Assurance Identification/Certification/Declaration
(Common Federal Rule)**

<p>Policy: Research activities involving human subjects may not be conducted or supported by the Departments and Agencies adopting the Common Rule (56FR28003, June 18, 1991) unless the activities are exempt from or approved in accordance with the common rule. See section 101(b) the common rule for exemptions. Institutions submitting applications or proposals for support must submit certification or appropriate Institutional Review Board (IRB) review and approval to the Department or Agency in accordance with the common rule.</p>	<p>Institutions with an assurance of compliance that covers the research to be conducted on file with the Department, Agency, or the Department of Health and Human Services (HHS) should submit certification of IRB review and approval with each application or proposal unless otherwise advised by the Department or Agency. Institutions which do not have such an assurance must submit an assurance and certification of IRB review and approval within 30 days of a written request from the Department or Agency.</p>
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<p>1. Request Type <input type="checkbox"/> ORIGINAL <input type="checkbox"/> FOLLOWUP <input type="checkbox"/> EXEMPTION</p>	<p>2. Type of Mechanism <input type="checkbox"/> GRANT <input type="checkbox"/> CONTRACT <input type="checkbox"/> FELLOWSHIP <input type="checkbox"/> COOPERATIVE AGREEMENT <input type="checkbox"/> OTHER: _____</p>	<p>3. Name of Federal Department or Agency and, if known, Application or Proposal Identification No.</p>
<p>4. Title of Application or Activity</p>		<p>5. Name of Principal Investigator, Program Director, Fellow, or Other</p>

6. Assurance Status of this Project (*Respond to one of the following*)

This Assurance, on file with Department of Health and Human Services, covers this activity:
Assurance identification no. M-_____ IRB identification no. _____

This Assurance, on file with (*agency/dept*) _____, covers this activity.
Assurance identification no. _____ IRB identification no. _____ (*if applicable*)

No assurance has been filed for this project. This institution declares that it will provide an Assurance and Certification of IRB review and approval upon request.

Exemption Status: Human subjects are involved, but this activity qualifies for exemption under Section 101(b), paragraph _____.

7. Certification of IRB Review (*Respond to one of the following IF you have an Assurance on file*)

This activity has been reviewed and approved by the IRB in accordance with the common rule and any other governing regulations or subparts on (*date*) _____ by: Full IRB Review or Expedited Review

This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by the common rule will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

8. Comments

<p>9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed and certification will be provided.</p>	<p>10. Name and Address of Institution</p>	
<p>11. Phone No. (<i>with area code</i>)</p>	<p>12. Fax No. (<i>with area code</i>)</p>	
<p>13. Name of Official</p>	<p>14. Title</p>	
<p>15. Signature</p>	<p>16. Date</p>	

Authorized for local Reproduction
Sponsored by HHS/NIH

OPTIONAL FORM 310 (Rev. 1-98)

Public reporting burden for this collection of information is estimated to average less than an hour per response. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: NIH, Project Clearance Office, 6701 Rockledge Drive, MSC 7730, Bethesda, MD 20892-7730, ATTN: PRA 0925-0418. Do not return the completed form to this address.

Appendix I

Research Involving Animals

Appendix I of this Announcement contains the required approvals, forms, and descriptions for research involving animals. Address all issues relating to the use of animals in the proposed research. Research conducted under sponsorship of the U.S. Army Medical Research and Materiel Command (USAMRMC) that generates pre-clinical safety data intended to support a research or marketing permit for products regulated by the Food and Drug Administration will be in conformance with the Good Laboratory Practices Regulations. Please note that Department of Defense (DOD) procedures for reviewing and approving the use of animals in research differ from those required by other funding agencies.

Table of Contents

<u>Part</u>	<u>Page</u>
1. Introduction	I-2
2. Alternatives to Painful Procedures	I-2
3. Rationale for Using Animals	I-2
4. Species Identification and Rationale	I-3
5. Rationale for the Number of Animals Required	I-3
6. Experimental Design	I-3
7. Anesthesia/Analgesia/Tranquilization	I-3
8. Study Endpoint	I-3
9. Euthanasia or Final Disposition	I-3
10. Institutional Animal Care and Use Committee(s) (IACUC) Approval	I-3
11. U.S. Department of Agriculture (USDA) Inspection Report	I-4
12. Qualifications	I-4
13. Accreditation	I-4
14. Principal Investigator Signed Assurances	I-4

Research Involving Animals

1. Introduction

If using animals, provide all information required by this appendix. Any and all subcontractors using animals must also provide the information required by this appendix.

Department of Defense (DOD) definition of **animal**: **Any live nonhuman vertebrate.**

The DOD Directive 3216.1, dated April 17, 1995, provides policy and requirements for the use of animals in DOD-funded research. **These requirements may differ from those of other funding agencies.** Each of the following items **must be** addressed in a proposal appendix entitled "Research Involving Animals." Questions concerning animal use should be directed to:

Fax: (301) 619-4165
Phone: (301) 619-2144
Mail: U.S. Army Medical Research and Materiel Command
ATTN: MCMR-RCQ-AR
504 Scott Street
Fort Detrick, MD 21702-5012

2. Alternatives to Painful Procedures

A painful procedure is defined as any procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being to which that procedure is applied. A written narrative description of the methods and sources used to search for alternatives to painful procedures, including alleviated pain, **must** be provided. The minimal written narrative must include: the databases searched or other sources consulted, the date of the search and the years covered by the search, and the key words and/or search strategy used by the Principal Investigator (PI) when considering alternatives or descriptions of other methods and sources used to determine that no alternatives were available to the painful or distressful procedure. Where Federal law requires specific testing procedures, the Code of Federal Regulations references or other legal guidelines requiring them should be noted. [The U.S. Army Medical Research and Materiel Command (USAMRMC) reserves the right to request evidence that a literature search for alternatives to painful procedures was performed.]

3. Rationale for Using Animals

Provide a rationale for using animals in the proposed research. Explain what alternatives to animal use were considered, such as computer modeling or cell cultures, and explain why these alternatives cannot be used to obtain the research objectives. **It is USAMRMC policy that alternatives to the use of animals be thoroughly investigated prior to submission of any proposal involving animals.**

4. Species Identification and Rationale

Identify the species of animals to be used and provide a rationale for their use. Explain why this particular animal model(s) was chosen over other animal models.

5. Rationale for the Number of Animals Required

Provide the **number of each species of animals** to be used by experimental design. Justify these numbers either **scientifically or mathematically**. **Show how these numbers were determined to be the minimum** required to obtain valid results.

6. Experimental Design

Provide a complete description of the proposed use of the animals by experimental design. Include surgical procedures, biosamples (frequency, volume, harvest site, and method of tissue collection), adjuvants, and other injections (agent, dosage, route, and anatomical site of administration).

7. Anesthesia/Analgesia/Tranquilization

Describe what anesthetics, tranquilizers, and analgesics will be used by agent, dosage, route, and anatomical site of administration. If none are to be used, provide an explanation.

8. Study Endpoint

Describe the projected endpoint or termination of the study for the animals.

9. Euthanasia or Final Disposition

Describe the method of euthanasia by agent, dosage, route, and anatomical site of administration. If animals are not euthanized, state final disposition of the animals.

10. Institutional Animal Care and Use Committee(s) (IACUC) Approval

Provide evidence of protocol approval from the IACUC of the institution where animal research will be performed including any subcontracting facility. If it was not possible to have the protocol reviewed by the Committee prior to submission of the proposal, then so state. Evidence of committee review can follow proposal submission, but must be provided prior to award.

RESEARCH WILL NOT BE FUNDED WITHOUT EVIDENCE OF APPROVAL FROM THE IACUC(s).

11. U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service Animal Care Inspection Report

Include a copy of the most recent USDA Inspection Report for any and all facilities where animal research will be performed, including any subcontracting facility.

12. Qualifications

Provide information on the qualifications and training of personnel performing the animal procedures. This information must specifically address the training and experience these personnel possess in using and manipulating the species of animals detailed in the proposal.

13. Accreditation

One of the following must be provided for each facility where the animal research will be conducted:

1. Evidence that the facility is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC-I).
2. A copy of the Institutional Letter of Assurance of Compliance with the “Public Health Service Policy on Humane Care and Use of Laboratory Animals,” revised September 1986.
3. A statement signed by the Institutional Official that the care and use of animals will be performed according to the National Research Council 1996 “Guide for the Care and Use of Laboratory Animals” and applicable Federal regulations.

14. Principal Investigator Signed Assurances

The PI must provide the following signed assurances (these pages may be photocopied and signed):

1. I assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research and that analgesic, anesthetic, and tranquilizing drugs will be used where indicated and appropriate to minimize discomfort and pain to animals.
2. I assure that the animals authorized for use in this protocol will be used only in the activities, manner, and quantities described herein, unless a deviation is specifically approved by my IACUC and the USAMRMC Animal Use Review Division.

Appendix I

3. I accept full responsibility for the proper care and use of the animals during the conduct of research outlined in the proposal.
4. I verify that I have made a reasonably good faith effort to ensure that this protocol is not an unnecessary duplication of previous experiments.
5. I verify that the personnel performing the animal procedures/manipulations described in this protocol are technically competent in those procedures and have received training on the use of animals in research as required by the Animal Welfare Act of 1985.
6. I assure that I have consulted with an individual who is qualified to evaluate the statistical design or strategy of this proposal and that the minimum number of animals needed for scientific validity will be used.

Principal Investigator's Signature

NOTE: For proposals that require the use of nonhuman primates, companion animals, marine mammals, or research deemed sensitive by the USAMRMC, a site visit shall be conducted as necessary by the USAMRMC Animal Use Review Officer or designees.

Appendix J

Safety Program Plan

Appendix J of this Announcement contains the required assurances, approvals, forms, and descriptions relating to safety.

Table of Contents

<u>Part</u>	<u>Page</u>
1. Affirmation of Safety	J-2
2. Research Operations/SOPs.....	J-2
3. Facility Equipment and Description.....	J-3
4. Hazard Analysis	J-3
5. Radioactive Materials.....	J-3
6. Recombinant DNA.....	J-3
7. Biological Defense Program Requirements	J-3

Safety Program Plan

Each of the applicable items below must be addressed in a proposal appendix entitled “Safety Program Plan” and must be prepared specifically for the proposal. Each section should be operation/research-specific and addressed in order.

Institutional safety manuals may be referenced; however, **do not send copies of Facility Safety Plans (FSPs) or Standard Operating Procedures (SOPs)**. A list of program contents with a brief description of each item (maximum 3 pages) is acceptable. If not applicable, so state. Provide a **website address**, if available, for additional safety and occupational health information.

Those items that do not apply to the proposed research will be labeled as “not applicable” or “N/A.”

1. Affirmation of Safety

The Principal Investigator (PI) (recipient) shall submit the following paragraph as affirmation that a safety program is in place and in accordance with all applicable regulations.

_____ affirms that there is an existing safety program that is in accordance with appropriate Federal, State, and Local regulations, as required by the Occupational Safety and Health Act; that hazards have been identified, eliminated, and/or controlled; and that research may be performed safely under laboratory conditions.

_____ shall be held responsible and liable for inaccuracies of the information provided, failure to implement an effective safety and occupational health program, and/or adverse conditions that may result from the failure of the recipient to identify hazard information.

Signature of Recipient, Date

2. Research Operations/SOPs

Safety procedures relating to the research operation. These should include but are not limited to the following: description of safety procedures for performing the protocol; description of any special skills and training to ensure safe research operations (Safety Committee, HAZCOM, Blood-borne Pathogen, and Chemical Hygiene, etc.); and description of medical surveillance and support.

3. Facility Equipment and Description

This should include a description of any biological safety cabinets, ventilation system employed, and personal protective equipment.

4. Hazard Analysis

Include a description of each hazard identified, hazard analysis based on maximum credible event, and plan to minimize or eliminate hazards (infection, toxic substance, and biological hazards).

5. Radioactive Materials

If radioactive materials are used, the materials and the disposal method should be identified. A copy of the Nuclear Regulatory Committee (NRC)-state-approved license or agreement shall be submitted. If no such material is to be used, it should be so stated.

6. Recombinant DNA

Research involving recombinant deoxyribonucleic acid (DNA) must meet or exceed National Institutes of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules, January 1997 edition. Include a written approval letter from the organization's Institutional Biosafety Committee (IBC). The IBC reviews all applications to perform protocols involving recombinant DNA (biohazardous material). If DNA experiments are exempt under the NIH Guidelines, include a copy of the written exemption notification. If not applicable, it should be so stated.

Copies of the NIH Guidelines are available at:

Fax: (301) 496-9839
Phone: (301) 496-9838
Website: www.nih.gov/od/ora
E-mail: lawsonb@od.nih.gov
Mail: Office of Recombinant DNA Activities
National Institutes of Health, MSC 7010
6000 Executive Boulevard, Suite 302
Bethesda, MD 20892-7010

7. Biological Defense Program Requirements

- Contractors performing work with **Biosafety Level-3 and 4** material must prepare a safety plan in accordance with 32 CFR 626.18.
- Local emergency support agencies, such as law enforcement, fire departments, health departments, and governments will be informed of Biological Defense Program (BDP)

activities and the appropriate support necessary, to include any equipment and training to provide effective emergency response. Agreements with external agencies must be formalized. (For the purpose of this requirement, the term “local emergency support agencies” refers to any agency that could reasonably be expected to have some capability to provide timely and effective support in the management or resolution of a biological mishap arising from BDP operations.) **A copy of this agreement must be submitted with the proposal.**

- **(Sample)**

Local Emergency Support

(Police, Fire, Health Department), is fully aware of the research program entitled _____ in the Department of _____ at _____, which is supported by the U.S. Army Medical Research and Materiel Command (Contract Number _____). In the event that a situation requires our response, we are equipped and prepared to handle those emergencies as appropriate for this project.

Acknowledged:

Name	Title (e.g., Fire Chief)	Date
------	--------------------------	------

- The PI is directly responsible and liable for all aspects of research project safety and ensures that all Facility Safety Plan requirements are in compliance with 32 CFR 626 and 627 (Biological Defense Safety Program and Biological Defense Safety Program, Technical Safety Requirements).

Appendix K

Representations and Certifications for Grants and Cooperative Agreements

Note: This form is to be completed by Contracting Office at Investigator's Institution or Agency.

1. CERTIFICATION REGARDING LOBBYING FOR GRANTS AND COOPERATIVE AGREEMENTS

Submission of this certification is required by Section 1352, Title 31 of the U.S. Code (USC) and is a prerequisite for making or entering into a grant or cooperative agreement over \$100,000.

The undersigned certifies, to the best of his or her knowledge and belief, that:

- (a) No Federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of an agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with the making of any Federal grant, the entering into of any cooperative agreement, and the extension, continuation, renewal, amendment, or modification of any Federal grant or cooperative agreement.
- (b) If any funds other than Federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with this Federal grant or cooperative agreement, the undersigned shall complete and submit Standard Form LLL, "Disclosure Form to Report Lobbying," in accordance with its instructions.
- (c) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers (including subgrants, contracts under grants and cooperative agreements, and subcontracts) and that all subrecipients shall certify and disclose accordingly.

This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into this transaction imposed by Section 1352, Title 31 USC. Any person who fails to file the required certification shall be subject to a civil penalty of not less than \$10,000 and not more than \$100,000 for each such failure.

(Organization Name)

(Agency Award Number)

(Name and Title of Authorized Representative)

Appendix K

Title of Research	Title of Research
Grants Officer's/Contracting Officer's Name	Grants Officer's/Contracting Officer's Name
Telephone No. and Area Code	Telephone No. and Area Code

5. NON-DELINQUENCY OF DEBT

The recipient certifies by signature on the award document that it is not delinquent in payment of any debt to the United States Government.

6. MILITARY RECRUITING ON CAMPUS (DOMESTIC EDUCATIONAL INSTITUTIONS ONLY)

As a condition for receipt of funds available to the Department of Defense (DOD) under this award, the recipient agrees that it is not an institution that has a policy of denying, and that it is not an institution that effectively prevents, the Secretary of Defense from obtaining for military recruiting purposes:

- (a) entry to campuses or access to students on campuses; or
- (b) access to directory information pertaining to students. If the recipient is determined, using procedures established by the Secretary of Defense to implement section 558 of Public Law (PL) 103-337 (1994), to be such an institution during the period of performance of this agreement, and therefore to be in breach of this clause, the Government will cease all payments of DOD funds under this agreement and all other DOD grants and cooperative agreements, and it may suspend or terminate such grants and agreements unilaterally for material failure to comply with the terms and conditions of award.

7. ASSURANCE OF COMPLIANCE WITH TITLE VI OF THE CIVIL RIGHTS ACT OF 1964.

_____ (Name of Applicant) hereby agrees that it complies with Title VI of the Civil Rights Act of 1964 (PL 88-352). In accordance with Title VI of that Act, no person in the United States shall, on the ground of race, color, or national origin, be excluded from participation in, be denied the benefits of, or otherwise subjected to discrimination under any program or activity for which the Applicant receives Federal financial assistance from the U.S. Government; and hereby gives assurance that it will immediately take any measures necessary to effectuate this agreement.

Appendix K

This assurance is given in consideration of and for the purpose of obtaining any and all Federal grants, cooperative agreements, loans, contracts, property, discounts or other Federal financial assistance extended after the date hereof to the Applicant by the U.S. Government, including installment payments after such date on account of applications for Federal financial assistance which were approved before such date. This assurance is binding on the Applicant, its successors, transferees, and assignees, and the person or persons whose signatures appear below are authorized to sign this Assurance on behalf of the Applicant.

Applicant (type or print)

Date

By _____
Signature and Title of Authorized Official

Applicant's mailing address

8. CERTIFICATION REGARDING DEBARMENT, SUSPENSION, PROPOSED DEBARMENT, AND OTHER RESPONSIBILITY MATTERS

- (a) (1) The Offeror certifies, to the best of its knowledge and belief, that--
 - (i) The Offeror and/or any of its Principals--
 - (A) Are Are Not, presently debarred, suspended, proposed for debarment, or declared ineligible for the award of contracts by any Federal agency;
 - (B) Have Have Not, within a three-year period preceding this offer, been convicted of or had a civil judgment rendered against them for: commission of fraud or a criminal offense in connection with obtaining, attempting to obtain, or performing a public (Federal, state, or local) contract or subcontract; violation of Federal or state antitrust statutes relating to the submission of offers; or commission of embezzlement, theft, forgery, bribery, falsification or destruction of records, making false statements, or receiving stolen property; and
 - (C) Are Are Not, presently indicted for, or otherwise criminally or civilly charged by a governmental entity with, commission of any of the offenses enumerated in subdivision (a)(1)(i)(B) of this provision.
 - (ii) The Offeror has has not, within a three-year period preceding this offer, had one or more contracts terminated for default by any Federal agency.
- (2) "Principals," for the purposes of this certification, means officers; directors; owners; partners; and, persons having primary management or supervisory responsibilities within a business entity (e.g., general manager; plant manager; head of a subsidiary, division, or business segment, and similar positions).

Appendix K

THIS CERTIFICATION CONCERNS A MATTER WITHIN THE JURISDICTION OF AN AGENCY OF THE UNITED STATES AND THE MAKING OF A FALSE, FICTITIOUS, OR FRAUDULENT CERTIFICATION MAY RENDER THE MAKER SUBJECT TO PROSECUTION UNDER SECTION 1001, TITLE 18, UNITED STATES CODE.

- (b) The Offeror shall provide immediate written notice to the Grants Officer/ Contracting Officer if, at any time prior to contract award, the Offeror learns that its certification was erroneous when submitted or has become erroneous by reason of changed circumstances.
- (c) A certification that any of the items in paragraph (a) of this provision exists will not necessarily result in withholding of an award under this solicitation. However, the certification will be considered in connection with a determination of the Offeror's responsibility. Failure of the Offeror to furnish a certification or provide such additional information as requested by the Grants Officer/ Contracting Officer may render the Offeror nonresponsible.
- (d) Nothing contained in the foregoing shall be construed to require establishment of a system of records in order to render, in good faith, the certification required by paragraph A of this provision. The knowledge and information of an Offeror is not required to exceed that which is normally possessed by a prudent person in the ordinary course of business dealings.
- (e) The certification in paragraph (a) of this provision is a material representation of fact upon which reliance was placed when making award. If it is later determined that the Offeror knowingly rendered an erroneous certification, in addition to other remedies available to the Government, the Grants Officer/Contracting Officer may terminate the contract resulting from this solicitation for default.

9. DATA UNIVERSAL NUMBERING SYSTEM (DUNS)

The Offeror is requested to provide the 9-digit DUNS number on the following line:

DUNS Number: _____

10. TAXPAYER IDENTIFICATION

- (a) Definitions.

“Common parent,” as used in this solicitation provision, means that corporate entity that owns or controls an affiliated group of corporations that files its Federal income tax returns on a consolidated basis, and of which the Offeror is a member.

Appendix K

“Corporate status,” as used in this solicitation provision, means a designation as to whether the Offeror is a corporate entity, an unincorporated entity (e.g., sole proprietorship or partnership), or a corporation providing medical and health care services.

“Taxpayer Identification Number (TIN),” as used in this solicitation provision, means the number required by the Internal Revenue Services (IRS) to be used by the Offeror in reporting income tax and other returns.

(b) All offerors are required to submit the information required in paragraphs (c) through (e) of this solicitation provision in order to comply with reporting requirements of 26 USC 6041, 6041A, and 6050M and comply with reporting requirements of 26 USC 6041, 6041A, and 6050M and implementing regulations issued by the IRS. If the resulting award is subject to the reporting requirements described in Federal Acquisition Regulations (FAR) 4.903, the failure or refusal by the Offeror to furnish the information may result in a 20 percent reduction of payments otherwise due under the contract.

(c) Taxpayer Identification Number (TIN)

TIN: _____

TIN has been applied for

TIN is not required because:

- Offeror is a nonresident alien, foreign corporation, or foreign partnership that does not have income effectively connected with the conduct of a trade or business in the U.S. and does not have an office or place of business or a fiscal paying agent in the U.S.;
- Offeror is an agency or instrumentality of a foreign government;
- Offeror is an agency or instrumentality of a Federal, state, or local government;
- Other. State basis.

(d) Corporate Status

- Corporation providing medical and health care services, or engaged in the billing and collecting of payments for such services;
- Other corporate entity;

Appendix K

- Not a corporate entity;
- Sole proprietorship;
- Partnership;
- Hospital or extended care facility described in 26 Code of Federal Regulations (CFR) 501(c)(3) that is exempt from taxation under 26 CFR 501(a).

(e) Common Parent

- Offeror is not owned or controlled by a common parent as defined in paragraph (a) of this clause.
- Name and TIN of common parent:

Name _____

TIN _____

11. INSTITUTION CODE

The Offeror is requested to provide its Federal Interagency Committee on Education (FICE) Institution Code on the following line:

Institution Code: _____

12. COMMERCIAL AND GOVERNMENT ENTITY (CAGE) CODE REPORTING

- (a) The Offeror is requested to enter its CAGE code on the following line and on its offer in the block with its name and address. The CAGE code entered must be for that name and address. Enter CAGE before the number.

CAGE Code: _____

- (b) If the Offeror does not have a CAGE code, it may ask the Grants Officer/Contracting Officer to request one from the Defense Logistics Services Center (DLSC).

- (c) The Grants Officer/Contracting Officer will--

- (1) Ask the Recipient to complete section B of a DD Form 2051, Request for Assignment of a CAGE Code;
- (2) Complete section A and forward the form to DLSC; and
- (3) Notify the Recipient of its assigned CAGE code.

Appendix K

(d) The offeror should not delay submission of the offer pending receipt of a CAGE code.

13. PAYMENT ADDRESS (MAR 1992) (USAMRAA)

In the event the offeror is awarded an agreement, the Offeror shall indicate below the address to which any payments should be mailed if that address is different from the mailing address shown for the Offeror:

Appendix L

General Information

Appendix L of this Announcement contains general information relating to U.S. Army Medical Research and Materiel (USAMRMC) policies and procedures.

Table of Contents

<u>Part</u>	<u>Page</u>
1. USAMRMC Award.....	L-2
2. Historically Black Colleges and Universities/Minority Institutions (HBCU/MIs).....	L-2
3. Procurement Integrity, Conflicts of Interest, and Other Improper Business Activities	L-2
4. Disclosure of Information Outside of the Government.....	L-2
5. Award Eligibility.....	L-2
6. Government Obligation.....	L-3
7. Information Service.....	L-3
8. Funding Instrument	L-3
9. Inquiry Review Panel (IRP)	L-3
10. Equipment/Property	L-4

General Information

1. USAMRMC Award

The USAMRMC implements its extramural research program predominantly through the award of grants and cooperative agreements. Proposals selected for funding are processed by the U.S. Army Medical Research Acquisition Activity (USAMRAA).

All awards are made to organizations, not individuals. A Principal Investigator (PI) should submit a proposal through, and be employed by or affiliated with, a university, college, nonprofit research institute, commercial firm, or Government agency (including military laboratories) in order to receive support.

2. Historically Black Colleges and Universities/Minority Institutions (HBCU/MIs)

Colleges and universities that qualify as HBCU/MIs are determined by the Department of Education (DOEd) to meet the requirements of Title 34 Code of Federal Regulations (CFR) Subpart 608.2 or 34 CFR Subpart 607.2. The official DOEd HBCU/MI list is posted on the CDMRP website. This list will be used to verify institutional HBCU/MI status. To access the list, go to <http://cdmrp.army.mil>, then select HBCU/MI list.

3. Procurement Integrity, Conflicts of Interest, and Other Improper Business Activities

The Procurement Integrity Act, Title 41 United States Code 423, et seq., contains prohibitions against certain activities between offerors and Government officials. Any questions regarding these prohibitions should be directed to the USAMRMC legal staff at (301) 619-2065. Proposed military/civilian collaborations should pay special attention to the Procurement Integrity Act.

4. Disclosure of Information Outside the Government

By submission of an application, the applicant understands that disclosure of information outside the Government shall be for the sole purpose of technical evaluation. The USAMRMC will obtain a written agreement from the evaluator that information in the proposal will only be used for evaluation purposes and will not be further disclosed or utilized. Funded projects may be subject to public release under the Freedom of Information Act; proposals that are not selected for funding will not be subject to public release.

5. Award Eligibility

To be eligible for award, a prospective recipient should meet certain minimum standards pertaining to institutional support, financial resources, prior record of performance, integrity,

organization, experience, operational controls, facilities, and conformance with safety and environmental statutes and regulations [Office of Management and Budget (OMB) Circular A-110].

6. Government Obligation

PIs are cautioned that only an appointed Contracting/Grant Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government to fund preparation of a proposal or to support research should be inferred from discussions with a technical project officer. A PI who, or an organization that, makes financial or other commitments for a research effort in the absence of an actual legal obligation signed by the USAMRAA Contracting/Grant Officer does so at their own risk.

7. Information Service

Offerors may use the technical reference facilities of the National Technical Information Service, 5285 Port Royal Road, Springfield, Virginia 22161, for the purpose of surveying existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. To the extent practical, all other sources should also be consulted for the same purpose.

8. Funding Instrument

All awards under this Announcement are anticipated to be grants or cooperative agreements.

More information on these funding instruments may be obtained on request from:

Fax: (301) 619-2937
E-mail: q&a.baa@det.amedd.army.mil
Mail: Director
U.S. Army Medical Research Acquisition Activity
ATTN: MCMR-AAA
Fort Detrick, MD 21702-5014

9. Inquiry Review Panel (IRP)

Applicants to this Announcement can submit a letter of inquiry to the USAMRMC in response to funding decisions made for a given proposal. Members of the Congressionally Directed Medical Research Programs staff, USAMRMC Judge Advocate General staff, and USAMRAA Grants Officers constitute an IRP and review each inquiry to determine whether factual or procedural errors in either peer or programmatic review have occurred, and if so, what action should be taken.

10. Equipment/Property

It is the policy of the Department of Defense that all commercial and nonprofit recipients possess the equipment and facilities needed to support proposed research. In those rare cases where specific additional equipment is approved for commercial and nonprofit organizations, such approved cost elements shall be separately negotiated.

Title to equipment or other tangible property purchased with grant or cooperative agreement funds may be vested in nonprofit institutions of higher education or with nonprofit organizations whose primary purpose is the conduct of scientific research. Normally, title will vest with the recipient organization, if vesting will facilitate scientific research performed by the institution or organization for the Government.

Appendix M

Acronyms Used in This Program Announcement

AAALAC-I	Association for Assessment and Accreditation of Laboratory Animal Care - International
AR	Army Regulation
ASCII	American Standard Code for Information Interchange
BCRP	Breast Cancer Research Program
BDP	Biological Defense Program
CAGE	Commercial and Government Entity
CDMRP	Congressionally Directed Medical Research Programs
CEQ	Council on Environmental Quality
CFR	Code of Federal Regulations
CR	Cancer Receptor
DA	Department of the Army
DHHS	Department of Health and Human Services
DLSC	Defense Logistics Services Center
DNA	Deoxyribonucleic acid
DOD	Department of Defense
DOEd	Department of Education
DUNS	Data Universal Numbering System
EPI	Environmental Process Interview
ET	Eastern Time
FAR	Federal Acquisition Regulations
FDA	Food and Drug Administration
FICE	Federal Interagency Committee on Education
FSP	Facility Safety Plan
FY	Fiscal year
HBCU	Historically Black Colleges and Universities
HBCU/MI	Historically Black Colleges and Universities/ Minority Institutions
HHS	Health and Human Services
HSPD	Human Subjects Protection Division
HSRRB	Human Subjects Research Review Board
IACUC	Institutional Animal Care and Use Committee
IBC	Institutional Biosafety Committee
IDE	Investigational Device Exemption
IND	Investigational New Drug
IP	Integration Panel
IRB	Institutional Review Board
IRP	Inquiry Review Panel
IRS	Internal Revenue Service

Appendix M

IUD	Intrauterine Device
MDR	Multi-Drug Resistance
MI	Minority Institution
MPA	Multiple Project Assurance
NDA	New Drug Application
NEPA	National Environmental Policy Act
NIH	National Institutes of Health
NRC	Nuclear Regulatory Committee
OCRP	Ovarian Cancer Research Program
ODCSRCQ	Office of the Deputy Chief of Staff for Regulatory Compliance and Quality
OF	Optional Form
OMB	Office of Management and Budget
OPRR	Office for Protection from Research Risks
OTSG	Office of The Surgeon General of the Army
PI	Principal Investigator
PL	Public Law
RCQ	Regulatory Compliance and Quality
RNA	Ribonucleic acid
SOP	Standard Operating Procedure
TIN	Taxpayer Identification Number
TSG	The Surgeon General
USAMRAA	U.S. Army Medical Research Acquisitions Activity
USAMRMC	U.S. Army Medical Research and Materiel Command
USC	United States Code
USDA	U.S. Department of Agriculture